# DETERMINING BODY MASS INDEX CUTOFFS TO IDENTIFY INCREASED RISK OF HYPERTENSION FOR ASIAN ETHNICITIES

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**ABSTRACT**

TUAN THANH NGUYEN: Determining Body Mass Index Cutoffs to Identify Increased Risk of Hypertension for Asian Ethnicities
(Under the direction of Barry M. Popkin, PhD)

An optimal BMI cutoff is needed in public health and clinical settings as the guidance an optimal body weight. Although body mass index (BMI) cutoffs of 25 and 30 kg/m$^2$ for overweight and obesity, respectively, have been widely used among Westerners and recommended by the World Health Organization as an international criterion for body fatness at the population level, there are still controversial opinions about the optimal BMI cutoffs for Asians. We conducted the study to determine an optimal BMI cutoff for overweight, which represents elevated hypertension and to determine the best anthropometric index in the prediction of hypertension in Asians. We used data from representative surveys conducted in China, Indonesia, and Vietnam in the early 2000s. With the use of ROC curve analyses, both longitudinal and cross-sectional studies suggest an optimal BMI cutoff of $< 25$ kg/m$^2$. The lower optimal BMI level is beneficial for Asians because it triggers earlier preventions for overweight and non-communicable diseases (NCDs), and thus, reduces economic and health burdens due to overweight and NCDs among Asians worldwide. In addition, our study shows ethnic differences in optimal BMI cutoffs between Chinese, Indonesian, and Vietnamese adults and suggests the use of country specific BMI cutoffs. We contribute to current knowledge by providing a BMI cutoff based on a longitudinal sample in Asians and a sample of Southeast Asians. With the use of the change-in-estimate approach, our findings show that

waist circumference does not perform better than BMI or adds meaningfully to the prediction of hypertension outcome by BMI. BMI appears to be sufficient to screen for cardiovascular risk in Asians.

## DEDICATION

I dedicate this work to my father, mother, wife, and son. The pursuit of my doctoral degree was only possible with their love, sacrifice, and support.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| AUC | area under the curve |
| BIA | bioelectrical impedance analysis |
| BMI | body mass index; |
| CHNS | the China Health and Nutrition Survey |
| CI | confidence intervals |
| DEXA | dual-energy x-ray absorptiometry |
| HC | hip circumference |
| IFLS | the Indonesia Family Life Survey |
| IOTF | International Obesity Taskforce |
| NCD | non-communicable disease |
| ROC | receiver operating characteristic |
| VNHS | the Vietnam National Health Survey |
| VNHS | the Vietnam National Health Survey |
| WC | waist circumference |
| WHO | the World Health Organization |
| WHR | waist-to-hip ratio |
| WSR | waist-to-stature ratio |

# CHAPTER 1. INTRODUCTION

## 1.1. Background

An optimal BMI cutoff is needed in public health and clinical settings as the guidance for people to maintain an optimal body weight. The effort is one of the strategies to control the increased prevalence of diseases, death, and economic burdens of overweight and non-communicable diseases (NCDs) are emerging problems in Asian countries. Although body mass index (BMI) cutoffs of 25 and 30 kg/m$^2$ for overweight and obesity, respectively, have been widely used among Westerners and recommended by the World Health Organization as an international criterion for body fatness at the population level, there are still controversial opinions about the optimal BMI cutoffs for Asians.

Differences in sampling and methods to determine an optimal BMI cutoff would lead to the differences in BMI cutoffs. Most of the work that serves as background for the debates about an optimal BMI cutoff for Asians used (a) cross-sectional samples and (b) a *P*-value or non-overlapping 95% confidence intervals (95% CI) as a decision rule. Because *P*-values and 95% CI widths are driven by both magnitude of effect and sample size, different conclusions could be the results of different sample sizes and BMI distributions. A BMI cutoff of 23 kg/m$^2$ was proposed by some authors, who used sensitivity, specificity, and receiver operating characteristic (ROC) curve analysis. These studies, however, were based on cross-sectional samples that did not ensure that the exposure to higher BMI had preceded hypertension outcome. Similar analysis with the use of a longitudinal sample is still needed.

To determine the best anthropometric index, the use of a *P*-value < 0.05, or a non-overlap of 95% CI is not adequate. Compared to BMI—a good indicator for body fatness in adults at the population level, waist circumference (WC), waist-to-stature ratio (WSR), and waist-to-hip ratio (WHR) provide additional information about central fat distribution. Studies aimed to determine whether WC, WHR, and WSR predict hypertension better than BMI or add to the prediction of hypertension have shown controversial results in both Western and Asian populations. As criteria for judging predictions of alternate indicators, these studies used a larger point estimate, a *P*-value < 0.05, or a non-overlap of 95% CI. The use of criteria that are less affected by sample size is still needed.

Because Asians are different from each other in many aspects, it is uncertain whether they have similar BMI and disease relationship. Asians have many sub-ethnic groups that are different in both individual and environmental background, such as body composition, genotypes, lifestyles, age structure, cultures, religions, and socio-economic status. Thus, we would expect to find ethnic differences in the association between BMI and disease risk within Asians. Current studies did not represent any Southeast Asian populations and did not allow direct comparison between different Asian ethnicities.

### 1.2. Research aims

The overall goal of the research was to determine an optimal BMI cutoff as a screening threshold for elevated hypertension in Chinese, Indonesian, and Vietnamese adults. Specific aims of this work were as follows:

***Aim 1.*** To compare the association between BMI and hypertension among 18–65-year-old Chinese, Indonesian, and Vietnamese adults; and to determine optimal BMI cutoffs for those populations. We hypothesized that Chinese, Indonesian, and Vietnamese adults require different optimal BMI cutoffs and respond differently to an increase in BMI. For this aim, we used three representative data sets: the China Health and Nutrition Survey in 2004 (CHNS 2004), the Indonesian Family Life Survey in 2000 (IFLS 2000), and the Vietnam National Health Survey in 2002 (VNHS 2002). We used Poisson regression models to examine the association between BMI and hypertension for each country. To define an optimal BMI cutoff, we computed and looked for the shortest distance on the ROC curve, estimated at each half unit of BMI.

***Aim 2.*** To determine an optimal BMI cutoff as a screening threshold for elevated incidence of hypertension in Chinese adults. We hypothesized that Chinese adults need an optimal BMI cutoff of less than 25 kg/m$^2$. For this aim, we used data from the CHNS 2000–2004 cohort. Cumulative incidence was calculated by dividing new cases of hypertension over the study period by the total at-risk population, aged 18–65 years, in 2000. Sex-specific ROC curves were used to assess the sensitivity and specificity of the BMI as a predictor of hypertension incidence.

***Aim 3.*** To compare the prediction of hypertension by WC, WSR, or WHR to that by BMI and to determine if WC, WSR, or WHR adds to the prediction of hypertension by BMI among 18–65-year-old Chinese adults. We hypothesized that at a population level, WC, WHR, and WSR do not add significantly to the prediction of hypertension by BMI. For this aim, we used data from the CHNS in 2004. A change of ≥ 10% in the prevalence ratio of BMI (PR) or area under the curve (AUC) when WC, WSR, or WHR was added to a model with BMI was used as the criterion for significant contribution to the prediction of hypertension by BMI. If AUC of WC, WSR, or WHR was ≥ 10% larger than that of BMI, it was considered as a better predictor.

# CHAPTER 2. LITERATURE REVIEW

## 2.1. Overweight and non-communicable diseases (NCDs) in developing countries

Overweight and obesity become emerging problems in almost all developing countries. National surveys in the late 1990s and the early 2000s showed a prevalence of overweight (BMI $\geq$ 25 kg/m$^2$) in adults of more than 50% in Mexico and more than 30% in Morocco, Brazil, Egypt, and South Africa (de Onis and Blossner 2000; Popkin 2002; Popkin 2006). The rates of increased obesity and overweight prevalence were varied and could go up to almost 2.5% annually in Mexico (Popkin 2002; Popkin 2006). In the 1990s, data from 94 developed and developing countries showed prevalence of overweight in preschoolers of at least 0.5% in all countries; two developed and 20 developing countries had the prevalence of 5% or greater (de Onis and Blossner 2000). Obesity is linked with increased health and economic burdens and reduced quality of life (Murray and Lopez 1997; Murray and Lopez 1997; Murray and Lopez 1997; Murray and Lopez 1997; de Onis and Blossner 2000; WHO 2003; Mendez, Monteiro et al. 2005).

Overweight is associated with increased risk of numerous NCDs such as hypertension, coronary heart diseases, heart failure, ischaemic stroke, type 2 diabetes mellitus, osteoarthritis, gout, renal failure, cancers, liver, and gall-bladder disorders. Modest weight reduction helps to reduce blood pressure and abnormal blood cholesterol and substantially lowers risk of type 2 diabetes (National Task Force on the Prevention and Treatment of Obesity 2000; WHO 2003; WHO/FAO expert consultation 2003). The 2002

World Heath Report shows that, about 58% of diabetes mellitus globally, 21% of ischaemic heart disease, and 8–42% of certain cancers were attributable to BMI of > 21 kg/$m^2$.

Hypertension is considered a good proxy indicator for cardiovascular diseases (CVDs) because elevated blood pressure levels produce an increased risk of CVDs. About 62% of cerebrovascular disease and 49% of ischaemic heart disease are attributable to systolic blood pressure of >115 mmHg). Furthermore, hypertension was ranked among top three of estimated attributable burdens in 2000, and projected to be an increased problem in 2010 and 2020 based on the Disability Adjusted Life Year (DALY) (WHO 2003). Blood pressure measurement could be done easily at a low cost that is considered a practical screening for CVDs in a developing country. Also, hypertension is a modifiable and treatable condition at an acceptable cost.

Increased BMI is associated with the increase in blood pressure in both adults and children (Iwao, Iwao et al. 2001; Colin Bell, Adair et al. 2002; Lin, Lee et al. 2002; Sorof, Lai et al. 2004; Wildman, Gu et al. 2004; Sakurai, Miura et al. 2006). Increased blood pressure is associated with the increase in BMI because higher BMI relates to higher body fluid volume, peripheral resistance (e.g., hyperinsulinemia, cell membrane alteration, and rennin-angiotensin excesses lead to functional constriction and structural hypertrophy), and cardiac output associated with weight gain (Kaplan 2006). An increase in BMI is also associated with an increase in visceral fat that leads to increased leptin and insulin resistance, worse lipid profiles, and increased progression of atherosclerosis and chronic renal failure (Kris-Etherton, Hecker et al. 2001; Forman and Bulwer 2006; Kaplan 2006; Pavey, Plalmer et al. 2006).

## 2.2. Ethnic differences in the association between BMI and NCDs

### *2.2.1. Asians differed from Westerners in the association between BMI and NCDs*

Asians are at higher risk of NCDs at a given BMI compared to Westerners. Bell et al (2002) found higher prevalence and odd ratio of hypertension at a given BMI among Chinese population compared to those of non-Hispanic White and non-Hispanic Black populations (Colin Bell, Adair et al. 2002). Jafar et al (2005) found that 5–14-year-old Pakistani children had higher BMI-adjusted blood pressure and hypertension prevalence compared to age and sex matched American children (Jafar, Islam et al. 2005). Also, findings from large-scale cross-sectional studies in Chinese and Indian populations suggested an optimal BMI cutoff of < 25 $kg/m^2$ (Bei-Fan 2002; Lin, Lee et al. 2002; Wildman, Gu et al. 2004; Mohan, Deepa et al. 2007). Huxley et al (2008), in a pulled sample of 263000 participants (73% Asian) from 21 cross-sectional studies in Australia and some Asian countries, also show an optimal BMI cutoff of about 24 $kg/m^2$ for Asians (Huxley, James et al. 2008).

There are several explanations for the lower optimal BMI cutoff for Asians compared to that of Westerners. First, Asian ethnicities tend to have a higher total body fat (Wang, Thornton et al. 1994; Deurenberg, Deurenberg-Yap et al. 2002) as well as a greater amount of abdominal and visceral fat (Park, Allison et al. 2001; Lear, Humphries et al. 2007) at a given BMI compared to other races and ethnicities. Increased visceral fat mass leads to increased blood pressure via leptin resistance, insulin resistance, and inflammation (Kaplan 2006; Sniderman, Bhopal et al. 2007). Second, ethnicities were usually associated with differences in socioeconomic status, cultural factors, food habits, physical activity levels, and lifestyles (Bell, Adair et al. 2004; Merlo, Asplund et al. 2004). Third, different ethnicities may have different combinations of genes associated with hypertension and gene-environment interactions that lead to the variation in phenotype of blood pressure (Carretero and Oparil 2000; Luft 2001; Maca-Meyer, Gonzalez et al. 2001; Cui, Hopper et al. 2002; Kaplan 2006). Finally, there is also speculation that any insults during fetal development and infancy might have also resulted in the elevated risks. However, there is great debate about these relationships and their subsequent effects (Barker 2002; Williams and Poulton 2002; Adair and Cole 2003; Demerath, Cameron et al. 2004; Singhal and Lucas 2004).

There are still some disagreements for a lower BMI cutoff in Asians. First, based on an increase in odd ratios or risk ratios, BMI cutoffs should be lower in all populations. Second, the use of different outcomes (risk factors, diseases, or mortality) would give different optimal BMI cutoffs; and it is difficult to defend the use of any one outcome over others. Also, different populations have very different educational levels, family medical history, fitness level as well as other characteristics. Those factors would bias the association between BMI and study outcomes (Stevens 2003). Stevens et al. (2002) had suggested a longitudinal study to directly compare the risk difference of different ethnic groups (Stevens, Juhaeri et al. 2002). In this study, we were not able to use this approach because we did not include any Western population in our sample. Also, mean BMI might be much lower in an Asian population compared to those of a Caucasian population. This difference in means would have lead to less-precise estimations at higher BMI among the Asians and at lower BMI among Caucasians.

#### *2.2.2. Asians differed from each other in the association between BMI and NCDs*

The finding that ethnicities modify the relationship between BMI and hypertension is not consistent within Asians. Bell et al (2002) found a higher prevalence and odd ratio (both crude and adjusted) of hypertension at a given BMI in Chinese women compared to those of Filipino women (Colin Bell, Adair et al. 2002). Comparing two East Asian countries, a study from Shiwaku et al (2004) showed that Mongolian adults had higher diastolic blood pressure, but lower systolic blood pressure at all level of BMI compared to Japanese adults, and recommended BMI cutoffs of 23 and 25 $kg/m^2$ to be used for Mongolian and Japanese adults, respectively (Shiwaku, Anuurad et al. 2004). Ito et al (2003), in a study involving 2728 Japanese 20-79 year-olds, suggested a BMI cutoff of 23.5 $kg/m^2$ for men and 22.5 $kg/m^2$ for women. Even different studies recommended different cutoffs for the Chinese population (Lin, Lee et al. 2002; Wildman, Gu et al. 2004; Weng, Liu et al. 2006). More research is needed to examine the ethnic differences in BMI – hypertension association within Asians.

There are several explanations for the differences in the associations between BMI and NCD risk within Asians. Asians are different from each other in their body mass index/body fat per cent relationship (Deurenberg, Yap et al. 1998; Deurenberg, Deurenberg-Yap et al. 2002). For example, at the same age, sex, and BMI, total body fat is highest in Indonesians, then Thais, and Chinese (Deurenberg, Yap et al. 1998); Indian Singaporeans have higher BF% than Malays Singaporeans, who in turn have a slightly higher BF% than Chinese Singaporeans; and Malays Indonesians have higher percent body fat compared to Chinese Indonesians (Deurenberg, Yap et al. 1998; Deurenberg, Deurenberg-Yap et al. 2002). Also, differences in genes, environment, and gene-environment interactions would be another potential explanation for the differences in the hypertension prevalence within Asians (Luft 2001; Maca-Meyer, Gonzalez et al. 2001; Bell, Adair et al. 2004; Merlo, Asplund et al. 2004; Macaulay, Hill et al. 2005; Misra and Ganda 2007; Razak, Anand et al. 2007).

In addition, the inconsistency in the BMI – hypertension association in Asians could be the result of differences in sampling and data analysis procedures. In the published studies, (a) sample size varied from less than 300 to more than 15000 for each ethnic group; and most of the studies were not nationally representative; (b) participant age, ranged from 18 to 87 year-olds, was varied from study to study; (c) BMI were categorized differently; and (d) methods to determine BMI cutoffs were also different: some authors compared the odd ratios or prevalence, while others used receiver operating characteristic (ROC) curve; some authors used multivariate models to adjust for confounding factors, the others did not. Further studies in with the use of ROC curve analyses in representative samples with a restriction in age (e.g., 18–65 years) are still needed. In addition, because the optimal BMI cutoffs for Asians are based largely on Chinese samples, the further study should also include a Southeast Asian population and should allow direct comparison between different Asian populations.

### 2.3. Prediction of hypertension by different anthropometric indices

#### *2.3.1. Fat mass and blood pressure*

Different types of body fat have different effect on disease risk. Fat is distributed into three main areas: subcutaneous, visceral, and other locations (e.g. retroperitoneal, perirenal and orbital). Visceral fat, drained by the portal vein and also known as organ fat, is located inside the peritoneal cavity, packed in between internal organs. Visceral fat is the most metabolically active fat and its accumulation is associated with increased risk of heart disease and type 2 diabetes (Govindarajan, Whaley-Connell et al. 2006). Leptin and insulin resistances as well as other inflammation factors explain how and why visceral fat associate with hypertension.

Leptin resistance is a cause of hypertension in over-fat people. Leptin, a 167-amino acid protein, is secreted from adipocytes, circulates in blood and binds to leptin receptor in the hypothalamus to reduce food intake and increase thermogenesis. Its net effect is to reduce body fat stores. Leptin produces both pressor and depressor actions. In a lean subject, leptin circulates in blood at a low level that leads to a normal blood pressure. Most of the obese subjects have an chronic hyperleptinemia that leads to leptin resistance (e.g., a decrease in transportation of leptin across the blood-brain barrier, a defect in the leptin receptor, or an impaired downstream signaling in the hypothalamus). The reduction in leptin function causes the retention of sodium, the decrease in insulin sensitivity, and the decrease in endothelial nitrite oxidization that lead to increased blood pressure (Haynes 2005; Rahmouni, Correia et al. 2005; Agapitov and Haynes 2006).

Besides leptin, adipocytes secrete other substances that cause elevated blood pressure. Adipocyte-derived hormones such as tumor necrosis factor- α (TNF-α), interleukin-6 (IL-6) and C-reactive protein also cause hypertension. TNF-α and IL-6, acting in peripheral tissues, modify metabolisms of energy, lipids, and carbohydrates. TNF-α, IL-6, and C-reactive protein, which cause systemic inflammation, alter cardiovascular structure and function. Most of adipose tissues, especially visceral fat, secrete blood pressure elevating factors such as angiotensinogen, angiotensin-converting enzyme and angiotensin $AT_1$ receptor. These factors could also act through insulin resistance to cause hypertension (Mark, Correia et al. 2004; Agapitov and Haynes 2006; Kaplan 2006).

Insulin resistance, a very common symptom in the over-fat, causes elevated blood pressure. Insulin resistance is associated with increased age, central adipose accumulation, excess food intake, low physical activity level, unhealthy lifestyles (e.g. smoking, alcohol drinking), and genetic factors. Insulin resistance causes hyperglycemia, dyslipidemia and hyperinsulinemia that, in their turns, cause sodium retention, increased sympathetic nervous system activity in brown adipose tissue, and vascular dysfunction, eventually leading to increased blood pressure (Kaplan 2006; Pavey, Plalmer et al. 2006).

### *2.3.2. Estimation of body composition in a population study*

Although lab-based methods provide valid and precise estimate of body composition, they are not applicable in a field study. The methods such as computerized tomography, magnetic resonance imagery, neutron activation analysis, densitometry, hydrometry, and dual-energy x-ray absorptiometry (DEXA) are usually used to obtain reference measures of body composition or to validate certain field based measurements. These methods, however, require very expensive equipments, high technical expertise, long time, and highly cooperated participants (Sutcliffe 1996; Ellis 2000; Gibson 2005).

Bioelectrical impedance analysis (BIA), a more practical method, shows some limitations. BIA is a rapid, safe, and relatively inexpensive method that has been widely used in evaluating body composition in field and clinical settings. It, however, requires good participant cooperation (e.g. no eating or drinking within 4 hours before the test, no alcohol consumption within 48 hours before the test, no exercise within 12 hours). Thus, it is difficult to be applied in a large scale survey especially in a developing country. BIA also shows other limitations: BIA does not provide information about regional fat; BIA has high standard error range with tendency to overestimate lean people and to underestimate obese people; and BIA uses equations (developed mainly based on Caucasian populations) that might not appropriate to Asians. Thus, BIA is not readily to be used in heterogeneous population with wide range of body fatness (Wang, Thornton et al. 1994; Baumgartner 1996; Sutcliffe 1996; Stolarczyk, Heyward et al. 1997; Ellis 2000; Gibson 2005).

Anthropometric measures and indices for body fat, such as weight, height, BMI, waist circumference (WC), waist-to-stature ratio (WSR), waist-to-hip ratio (WHR), and skinfold thickness are widely used to assess body composition and to predict chronic disease risk in individual and population levels. In a large-scale study, anthropometric indices show several advantages such as (a) procedures are simple, safe, and noninvasive; (b) equipment is inexpensive, portable, durable, and can be made or purchased locally; (c) measurements do not require high technical expertise; and (d) can be used to evaluate changes in nutrition status over time. However, the use of anthropometric indices shows certain limitations such as measurement errors (random and systematic), changes in composition and properties of certain tissues, and uses of invalid assumptions and models to interpret anthropometric measures or indices (Gibson 2005).

BMI, a height adjusted weight index, is a good indicator for body fatness in adults at the population level. Compared to other anthropometric indices, height and weight and thus BMI (a) are collected more often in nutrition and health surveys, interventions, and in clinics, (b) are collected with the use of universally accepted protocols, and (c) are easier to interpret. BMI correlates well with total body fat from a DEXA measure (correlation coefficient r of 0.75 or more in both younger and older adults; and in both men and women) (Hannan, Wrate et al. 1995; Gallagher, Visser et al. 1996; Morabia, Ross et al. 1999; Gibson 2005). BMI, however, is not able to distinguish between muscle and fat mass or to provide information about fat distribution.

WC, WSR, WHR, and skinfold thickness provide additional information about central fat distribution.(Gibson 2005; Klein, Allison et al. 2007) Those measurements or indices are commonly used to suggest whether an elevated BMI is associated with excessive adiposity (WHO expert committee 1995). WC is recommended by National Institute of Health (NIH) to assess abdominal fat. WC is especially informative among the normal weight or overweight (BMI from 18.5–24.9kg/m$^2$); while hip circumference (HC) and WHR are considered less informative (National Institute of Health 2000). There are some technical issues relating the use of WC: (a) there is no universally accepted sites for measuring WC that could yield considerable measurement errors; (b) there is a large variation in WC optimal cutoffs by sex, age, races, ethnicities, BMI levels, and health outcomes of interest; and (c) it does not distinguish among subcutaneous, visceral, and retroperitoneal fats (Wang, Thornton et al. 2003; Gibson 2005). Skinfold thickness, WC, and HC are more difficult to be measured compared to weight and height, because they have higher level of measurement errors, require more body exposure, additional equipments, and training.

#### *2.3.3. Prediction of hypertension by different anthropometric indices*

Inconsistent findings were reported among Caucasian populations about the single best anthropometric index for the prediction of CVD risk. WC is better than BMI in Italians (Guagnano, Ballone et al. 2001), Baltimorean adults aged < 65 years (Iwao, Iwao et al. 2001), Caucasians participating in NHANES III (Zhu, Wang et al. 2002), and Norfolk adults in United Kingdom (Canoy, Luben et al. 2004). Other studies suggest the use of both WC and BMI (Ardern, Katzmarzyk et al. 2003; Ardern, Janssen et al. 2004; Zhu, Heshka et al. 2004). WC is found to have similar prediction of CVD risk compared to BMI in Australian men (Dalton, Cameron et al. 2003), Baltimorean adults aged ≥ 65 years (Iwao, Iwao et al. 2001), German men aged 40–65 years and women aged 35–65 years (Kroke, Bergmann et al. 1998), American men participating in ERIC study (Harris, Stevens et al. 2000), and German adults participating in the Kiel Obesity Prevention Study (Bosy-Westphal, Geisler et al. 2006). WC is worse than BMI in Greek women (Benetou, Bamia et al. 2004), American women participating in ERIC study (Harris, Stevens et al. 2000), and Australian women (Dalton, Cameron et al. 2003). WC adds to the prediction of CVD risk by BMI among the normal and overweight (BMI from 18.5–29.9 $kg/m^2$) but not the obese (National Institute of Health 2000).

Studies in Asian populations also show inconsistent results about the single body fatness index for the prediction of hypertension. Wildman et al (2004 and 2005) found that although blood pressure was more strongly associated with BMI than WC, both BMI and WC are important indices in predicting hypertension outcome. However, the study did not cover the 18–34 year-olds; and the inclusion of the 65–74 year-olds might not be appropriate because BMI is not a good indicator for nutrition status of the older adults (WHO expert committee 1995). Some studies show that WC has similar or better prediction of hypertension in certain segments of population. WC shows a larger correlation with blood pressure compared to BMI and WHR in 25–74-year-old women; it, however, shows similar correlation in men (Ho, Chen et al. 2001). Similar predictions of hypertension by BMI, WC, and WHR were found in Taiwanese and Japanese adults (Lin, Lee et al. 2002; Ito, Nakasuga et al. 2003). The inconsistency in the association between different anthropometric indices and blood pressure needs further clarification.

It is still unclear if WSR predicts hypertension better than WC and BMI. Some authors recommended the use of WSR, instead of WC, in a population with a wide range in heights (Hsieh and Yoshinaga 1995; Ho, Lam et al. 2003; Hsieh, Yoshinaga et al. 2003; Sakurai, Miura et al. 2006). Hsieh and Yoshinaga (1995) found that WSR predicted better CVD risk factors than BMI and WHR among 20–78-year-old Japanese women (Hsieh, Yoshinaga et al. 2003). Furthermore, Hsieh et al (2003) in a study that involved Japanese 6141 men and 2137 women in Tokyo found that WSR was a practical index for assessing central fat distribution and metabolic risk among both men and women. The authors suggested the use of 0.5 as WSR cutoff to identify high central fat distribution for both sexes (Hsieh, Yoshinaga et al. 2003). In another study involving 1412 men and 1483 women aged 25–74 years in Hong Kong, Ho et al (2003) compared BMI, WC, WHR, and WSR in the prediction of CVD risks. The BMI, WC, WSR, and WHR predicted well the CVD risks; WSR appeared the best predictor of cardiovascular risks (Ho, Lam et al. 2003). Study by Sakurai et al (2006), showed that WC, WSR, BMI, and WHR had equal prediction of hypertension among 35-59-year-old man workers; while BMI provided highest prediction among 35-59-year-old woman workers (Sakurai, Miura et al. 2006).

These inconsistent findings would be the results of the differences in methods to evaluate the prediction of BMI, WC, WSR, and WHR. Ho et al (2001) used partial correlation analysis to quantify the independent associations of the three anthropometric indices with hypertension, controlled for age and for each of these indices (Ho, Chen et al. 2001). Some authors used logistic regression controlling for potential confounder including the other anthropometric indices (Ho, Chen et al. 2001; Wildman, Gu et al. 2005). Some authors compared the absolute values of AUCs of ROC curves (Lin, Lee et al. 2002; Ito, Nakasuga et al. 2003) or used McNemer's $\chi^2$ to compare the distribution of true positives and negatives with that of false positives and negatives between two indices for obesity (Ito, Nakasuga et al. 2003).

In addition, as criteria for judging predictions of alternate indicators, those studies used a larger point estimate, a $P$-value < 0.05, or a non-overlap of 95% CI (Visscher, Seidell et al. 2001; Zhu, Wang et al. 2002; Benetou, Bamia et al. 2004) (Ho, Chen et al. 2001; Lin, Lee et al. 2002; Ho, Lam et al. 2003; Hsieh, Yoshinaga et al. 2003; Ito, Nakasuga et al. 2003; Wildman, Gu et al. 2005; Sakurai, Miura et al. 2006). Again, because $P$-values and 95% CI are driven by both magnitude of effect and sample size (Weinberg 2001), different conclusions would result from different sample sizes or BMI distributions. The use of other criteria that is less affected by sample size is still needed.

## 2.4. Longitudinal association between BMI and hypertension

### *2.4.1. Longitudinal association between BMI and hypertension*

A longitudinal study is a better study design to evaluate causation association compared to a cross-sectional study. Cross-sectional studies are usually used to evaluate prevalence and to generate a hypothesis. Because both exposure and outcome are evaluated at the same time, a cross-sectional study is not able to test a temporary criterion for a causal relationship (Grimes and Schulz 2002; Grimes and Schulz 2002). For example, a higher BMI is associated with an increase in blood pressure; however, a hypertensive patient would have modified his lifestyles that lead to a reduction of body weight, and thus BMI. A longitudinal study follows a disease-free population that is at different levels of an exposure, and estimates an outcome during the time of follow up. Thus, longitudinal study allows researchers to evaluate temporary criteria, to better control for potential confounding factors, and to estimate incidence, risk, risk ratios, and risk differences. A longitudinal study, however, also has some limitations: it (a) tends to be affected by selection bias, information bias, confounding factors, and loss of follow up; (b) is not usually generalizable to the whole population; and (c) is expensive and impractical in the context of a developing country (Grimes and Schulz 2002; Grimes and Schulz 2002).

There is limited number of studies evaluating the association between BMI and hypertension using data from a longitudinal study. Adair (2004) found a rapid increase in prevalence of overweight and obesity in Filipino women participating in the Cebu Longitudinal Health and Nutrition Survey from 1991 to 2000. The study aimed to explain the trend of BMI; it also explored how overweight and obesity affect prevalence of hypertension at the end of this interval. The study showed elevated risk of hypertension associate with high WHR and BMI (Adair 2004). However, the association between BMI and hypertension was only evaluate based on the last survey, thus the effect BMI on hypertension incidence is still unknown. Stevens et al (2002) used data from Cancer Prevention Study I (CPS-I) and the Atherosclerosis Risk in Communities (ARIC) to define BMI cutoffs for African American women that corresponding to a BMI of 30 $kg/m^2$ in Caucasian women. The study found that the use of different decision rules (e.g., incidence rate, rate ratio, and rate) gave difference conclusion about the BMI cutoffs for African American women (Stevens, Juhaeri et al. 2002).

### *2.4.2. Optimal BMI cutoffs based on longitudinal samples*

Optimal BMI levels based on all-cause mortality were derived from some longitudinal studies. BMI levels of 25 and 30 kg/m$^2$ for overweight and obesity, respectively, were based on a meta-analysis of 19 longitudinal studies for the association between BMI and all-causes mortality in Caucasian populations (about half were from the USA) (Troiano, Frongillo et al. 1996). Then, the BMI levels were recommended by the World Health Organization (WHO) as universal BMI cutoffs (WHO expert committee 1995; WHO expert consultation 2004). In two longitudinal study in Chinese population, a BMI of 24–24.9 kg/m$^2$ in men and 25–26.9 kg/m$^2$ in women (Gu, He et al. 2006) or of 24–27.9 kg/m$^2$ in both sexes (Zhou 2002) were associated with the lowest mortality rate.

The use of all-cause mortality as a study outcome shows some limitations: mortality can be extreme and influenced by factors other than BMI (e.g., morbidity, HIV/AIDS, pre-existing health condition, smoking, alcohol consumption, other lifestyles factors, accidents, suicides, and health care services) that are so different between developed and developing countries (Misra 2003). An outcome (e.g., cardiovascular risk or morbidity) that captures years of healthy, functional, high-quality life would be more beneficial (Misra 2003; Stevens 2003). We expect to see a higher BMI cutoff for an all-cause mortality outcome compared to hypertension or other cardiovascular risk because death is usually an advanced stage of diseases and not all causes of death are associated with an overweight status.

In addition, it is not sufficient to base on only the shape of the association between BMI and all-cause mortality. In those studies, the definition of optimal BMI levels was based on the lowest death rates across the BMI range. However, the death rates were only slightly less (most of them had overlap 95% CI or $P$-values $< 0.05$) than those with a higher or lower

BMI value (Troiano, Frongillo et al. 1996; Zhou 2002; Gu, He et al. 2006). A study that uses an ROC curve analysis to examine the sensitivities and specificities of different BMI levels for the prediction of a health risk is still needed.

### 2.5. Summary and significance

Nutrition and health transition is a period of both challenges and opportunities. In the last decades, China, Indonesia, and Vietnam are experiencing rapid economic growth. The economic growth helps to reduce the magnitudes of poverty, underweight, micronutrient deficiencies, and infectious diseases. On the other hand, changes in environments, dietary intakes, physical activities, and lifestyles have brought along increases in overweight and non-communicable diseases such as type 2 diabetes, cardiovascular diseases, and cancers. Thus, while underweight, micronutrient deficiencies, and communicable diseases are still notable issues, overweight and NCDs are becoming emerging problems in developing countries. However, at their early or middle stage of nutrition and health transitions, those countries also have a unique opportunity to reduce health and economic burdens attributed to overweight and non-communicable diseases.

In this research, we determined the most appropriate anthropometric index to screen for elevated risk of cardiovascular diseases and determined an optimal BMI cutoff for Chinese, Indonesian, and Vietnamese populations. To address these research questions, our study showed several innovation approaches and contributions.

Different Asian populations have been included in our sample. Asians have many sub-ethnic groups that are different in both individual and environmental backgrounds such as body compositions, genotypes, lifestyles, age structures, cultures, religions, and socio-economic status. Thus, we would expect to find ethnic differences in the association between BMI and disease risk within Asians. Also, current BMI cutoffs for Asians are based largely on the Chinese and Indians (East and South Asians). Our study enriched current knowledge by providing optimal BMI cutoffs for Southeast Asian populations. Because our study allows direct comparison between the Chinese, Indonesians, and Vietnamese, we could also examine whether a country-specific or even country-, sex-, age-specific BMI cutoffs are needed.

We are the first to use an ROC curve to evaluate the BMI cutoffs in an Asian longitudinal sample (the CNHS 2000–2004). From this cohort, we were able to estimate an optimal BMI cutoff based cumulative incidence of hypertension. It is also a unique opportunity for us to compare an optimal BMI cutoffs based on this longitudinal sample to those obtained from a cross-sectional sample (the CNHS in 2004). The comparison would suggest a certain adjustment to an optimal BMI level obtained from a cross-sectional study. The information is needed to develop an optimal BMI cutoff for a population where a longitudinal sample is not available.

In the context of a developing country, it is important to find a small number of practical, low cost, and culturally accepted anthropometric indices to predict elevated disease risk. Our study compared the prediction of hypertension by WC, WSR, or WHR to that by BMI and determined if WC, WSR, or WHR adds to the prediction of hypertension by BMI among Chinese adults. The effort help to determine the best anthropometric index screen for cardiovascular risk. We are the first to use the change-in-estimate approach that is more stable to sample sizes compared to methods that had been used by other authors (e.g., a *P*-value < 0.05 or a non-overlap of 95% CI).

# CHAPTER 3. RESEARCH DESIGN AND METHODS

## 3.1. Overview of study design and sample

### *3.1.1. The China Health and Nutrition Surveys*

The China Health and Nutrition Survey (CHNS), an ongoing study established in the late 1980s in nine provinces that vary substantially in geography, economic development, public resources, and health indicators. The sample (representing about 57% Chinese population) was based on a stratified, three-stage sample design; sampling weights, however, were not given to any households and individuals. A detailed description of study design and data collection procedures has been described elsewhere (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). For this research, we used data from CHNS in 2000 and 2004. Data sets and questionnaires may be downloaded from the CHNS websites (http://www.cpc.unc.edu/china).

### *3.1.2. The Indonesian Family Life Survey*

The Indonesia Family Life Survey (IFLS) is a continuing longitudinal socioeconomic and health survey established in 1993 in thirteen provinces that vary substantially in geography, economic development, public resources, and health indicators. The sample (representing about 83% Indonesian population) was based on a stratified, three-stage sample design; sampling weights were given to each household and individual (Strauss, Beegle et al. 2004). For this research, we used data from the third wave of IFLS conducted in 2000. Data sets and questionnaires may be downloaded from the IFLS websites (http://www.rand.org/labor/FLS/IFLS/).

### *3.1.3. The Vietnam National Health Survey*

The Vietnam National Health Survey (VNHS) is a nationally representative health survey conducted in Vietnam in 2002 in all 61 provinces in Vietnam. The survey was based on a stratified, three-stage sample design; sampling weights were given to each household and individual. A detailed description of study design and data collection procedures has been described elsewhere (Ministry of Health - General Statistical Office 2003; Tuan, Tuong et al. 2008). Information about data sets and questionnaires may be obtained from the Vietnam Ministry of Health (http://www.moh.gov.vn/solieu/defaultE.htm)

### *3.1.4. Exclusions*

We excluded participants who were pregnant or lactating at the time of survey; and for whom measurements of weight, height, or blood pressure were incomplete or implausible (e.g., BMI < 15 or > 35 kg/m$^2$; weight < 30 or > 150 kg; height < 130 or > 190 cm; and the difference between systolic and diastolic blood pressure < 10 mmHg). We also excluded participants with missing or implausible value of waist circumference (WC) or hip circumference (HC) (e.g., WC < 45 or >150 cm; HC < 55 or > 155 cm; or waist-to-hip ratio < 0.6 or > 1.1) in one manuscript.

We only included 18–65-year-old adults, non-pregnant, and non-lactating women because a teenager, an older person, or a pregnant or lactating woman requires different BMI cutoffs (WHO expert committee 1995). The exclusion of participants with missing values in key variables helped to maintain consistent sample sizes. The exclusion of participants with extreme or implausible values in anthropometric or blood pressure measurements helped to increase the estimate precision without changing the overall results.

## 3.2. Measurement of key variables

### *3.2.1. Blood pressure*

Blood pressure measurements were taken in a seated position and on the right arm by trained health workers who followed a standardized procedure using regularly calibrated mercury sphygmomanometers (CHNS), Omron digital devices (IFLS), or aneroid manometers (VNHS). In the CHNS and VNHS, systolic blood pressure was measured at the first appearance of a pulse sound (Korotkoff phase 1) and diastolic blood pressure at the disappearance of the pulse sound (Korotkoff phase 5); three measurements of systolic or diastolic blood pressure were averaged to reduce the effect of measurement errors. In the IFLS, systolic and diastolic blood pressures were obtained from the digital device (Popkin, Paeratakul et al. 1995; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004).

Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed by a doctor (Chobanian, Bakris et al. 2003). The definition of hypertension was not based on the use of an antihypertensive medication because (a) the information was not available in the VNHS and IFLS; and (b) a small proportion of Chinese adults was diagnosed (< 7%) or treated (< 5%) with any antihypertensive medication and none used antihypertensive medication without being diagnosed by a doctor.

Prevalence of hypertension was calculated by dividing current cases of hypertension by the total population. In the CHNS 2000–2004 cohort, cumulative incidence was calculated by dividing new cases of hypertension over the study period by the total at-risk population, aged 18–65 years, in 2000. In the analyses, we also presented adjusted prevalence or incidence of hypertension with adjustment for certain covariates.

### *3.2.2. Anthopometric measures and indices*

A BMI (kg/m$^2$) was calculated based on weight and height measured by trained health workers who followed standardized procedures using regularly calibrated equipment. The CHNS used SECA 880 scales and SECA 206 wall-mounted metal tapes; the IFLS and VNHS used SECA 890 scales and Shorr measuring boards (Popkin, Paeratakul et al. 1995; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004).

In the CHNS, the health workers used non-elastic tape to measure WC at a point midway between the lowest rib and the iliac crest in a horizontal plane and HC at the point yielding the maximum circumference over the buttocks (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). Waist-to-stature ratio (WSR = WC / height) and waist-to-hip ratio (WHR = WC / HC) were calculated based on the measured WC, height, and HC.

### *3.2.3. Covariates*

Covariates, such as age, sex, smoking habits, alcohol consumption, and place of residence were collected by direct interviews. Age was used as study covariates because they are both associate with BMI and blood pressure. In regression models, age was kept in continuous scale (e.g., age center at 40 years). Sex was used as study covariates because they are both associate with BMI and blood pressure. Almost all of the analyses in the research were stratified by sex.

Smoking habit was used in the analysis as a covariate because smoking associates with increased blood pressure, decreased BMI for current smoker, and increased BMI for ex-smoker. Number of cigarettes and pipes each day were collected in all surveys. Because the number of cigarettes and pipes were affected largely by rounding habit, and it is impossible to have any conversion between a cigarette and a pipe, we categorized smoking status to three categories: current smoker, former smoker, and never smoker to make it comparable among the surveys.

Alcohol drinking habit was used in the analysis as a covariate because it associates with both BMI (via energy intake) and blood pressure. Numbers and types of drink (beer, wine, and liquor) were only collected in CHNS 2000 and 2004. In VNHS 2002, only information about current drinking status was collected; in IFLS 2000, no information about alcohol drinking was collected. Thus, we used current drinking status (yes or no) as a covariate in the study.

Place of residence (urban or rural) could be considered as a confounder because of its indirect association with BMI and blood pressure via several unmeasured covariates (e.g. socio-economic status, lifestyle, jobs, assess to foods, and health services). We could not create urban index, so, the definition / characteristics of urban or rural might vary within and between countries.

Physical activity and food intakes are potential confounding factors of the association between BMI and hypertension because of its association with BMI and blood pressure. Because the information about physical activity and dietary intake was not detail enough to estimate habitual energy expenditure, energy intake, or nutrient intakes (e.g., sodium, potassium, fats, dietary fiber, or antioxidants), we did not include it in our analyses.

We did not include household economic status, education level, and jobs of respondents because they are not directly associated with outcome or main exposure and the definitions of those variables varied from study to study. Other covariates such as level of stress endured by jobs and living conditions, family history of hypertension, genetic factors, and biomarkers (e.g. insulin, glucose, and leptin levels) were not collected in any surveys.

### 3.3. Analytical strategy

Detail description of statistical analyses was presented in each manuscript. In summary, the analyses were conducted separately for each country with the use of survey and weighted commands, when appropriate. Missing and implausible values were identified and were either imputed or treated as missing data.

To determine an optimal BMI cutoff we conducted an receiver operating characteristic (ROC) curve analysis (for a maximized combination of sensitivity and specificity); to define the best anthropometric index in the prediction of hypertension, we used a change in estimates (e.g., prevalence ratios, or area under the curves). In addition, to make our finding comparable with those of other authors, we presented both crude and adjusted estimates with 95% CI; we also used a $P$-value $< 0.05$ to define a significant difference between groups. All analyses were performed with the use of Stata software version 9.2.

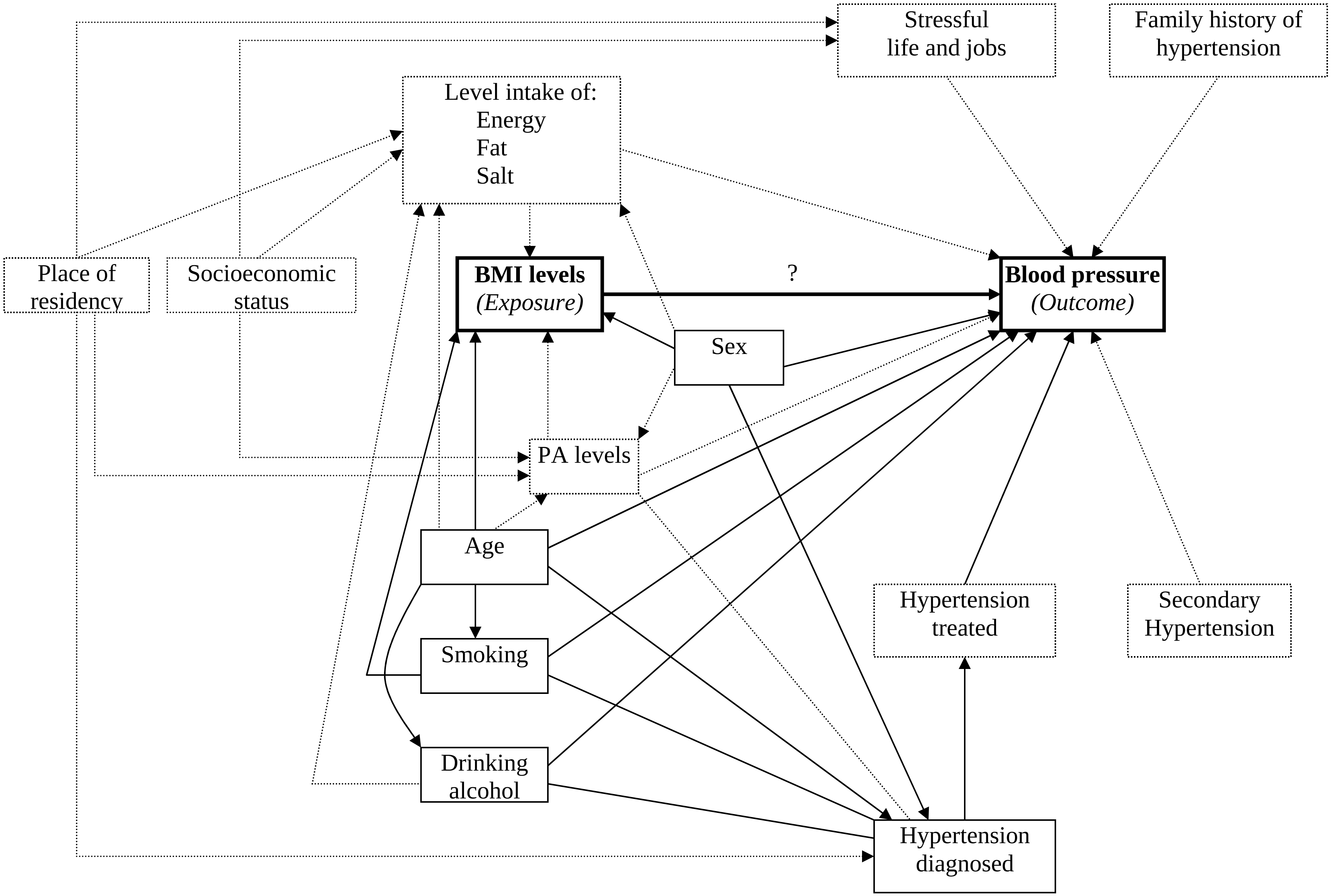


**Figure 3.1.** The association between BMI, hypertension, and other covariates
BMI, Body Mass Index (kg/m$^2$); PA, physical activity;
Solid line; measured variable/association; dashed line, un-measured variable/association

# CHAPTER 4. EAST AND SOUTHEAST ASIANS ARE DIFFERENT IN THE ASSOCIATION BETWEEN BODY MASS INDEX AND HYPERTENSION

## 4.1. Abstract

*Background:* Information about the association between body mass index (BMI) and chronic diseases in Asians was based largely on East and South Asian populations.

*Objective:* To determine the BMI and hypertension association in 18- to 65-y-old Chinese, Indonesian, and Vietnamese adults and to determine optimal BMI cutoffs for overweight in those populations.

*Design:* Population-based, cross-sectional study.

*Subjects:* 7562 Chinese, 18502 Indonesian, and 77758 Vietnamese participants aged 18- to 65 y.

*Measurements:* Blood pressure, weight, and height were measured by trained health workers. To define an optimal BMI cutoff, we computed and searched for the shortest distance on the receiver operating characteristic curve, estimated at one-half unit of BMI.

*Results:* Despite a low mean BMI, the prevalence of hypertension in Chinese, Indonesian, and Vietnamese men was 22.9, 24.8, and 14.4%, and women was 16.6, 26.9, and 11.7%, respectively. At all BMI levels, sex-specific prevalence of hypertension was highest in Indonesian adults compared to those of Chinese and Vietnamese adults ($P < 0.05$ at almost all BMI levels). The overall and stratified analyses suggested an optimal BMI cutoff of 23–24, 21–22.5, and 20.5–21 kg/m$^2$ for Chinese, Indonesian, and Vietnamese adults,

respectively. For each ethnicity, the cutoffs were about 0.5–1.0 unit higher in women compared to men and in the older (41- to 65-y-old) compared to the younger (18- to 40-y-old) participants.

*Conclusion:* The study showed an ethnic difference in the BMI-hypertension association and in the optimal BMI cutoffs for overweight in Chinese, Indonesian, and Vietnamese adults. Country-specific or even country-, sex-, and age-specific BMI cutoffs might be needed to identify people at high risk of cardiovascular diseases.

**4.2. Background**

Asian populations tend to develop chronic diseases at a lower body mass index (BMI) compared to other races and ethnicities (e.g., White, Hispanic, Black, and Polynesian) (WHO expert consultation 2004). The main explanation for the ethnic difference is that Asians tend to have higher total body fat, abdominal and visceral fat at a given BMI compared to other races and ethnicities (Wang, Thornton et al. 1994; Deurenberg, Deurenberg-Yap et al. 2002). Asians, however, have many sub-ethnic groups that are different in body composition, genotypes, age structure, lifestyles, cultures, religions, and socio-economic status (Deurenberg, Deurenberg-Yap et al. 2002; Macaulay, Hill et al. 2005). Thus, we would expect to find ethnic differences in the association between BMI and disease risk within Asians.

Although a BMI cutoff of 23 km/m$^2$ have been widely used to identify moderate to high risk of cardiovascular diseases in Asians (WHO expert consultation 2004), it is still unknown whether different Asian populations need different BMI cutoffs for overweight. A BMI cutoff of 23–24 kg/m$^2$ has been proposed by some authors who used sensitivity, specificity, and receiver operating characteristic (ROC) curve analysis in Chinese (Bei-Fan

2002; Lin, Lee et al. 2002; Ho, Lam et al. 2003; Wildman, Gu et al. 2004) and Indian (Mohan, Deepa et al. 2007) populations. However, these studies did not represent any Southeast Asian populations. The study by Huxley et al. (Huxley, James et al. 2008), which included a pooled sample of East, South, Southeast, and Middle East Asian populations, showed an optimal BMI cutoff for overweight of about 24 kg/m$^2$. The analysis, however, did not allow direct comparisons of the optimal BMI cutoffs in different Asian populations. Our study compared the association of BMI to hypertension in 18- to 65-y-old Chinese, Indonesian, and Vietnamese adults and determined optimal BMI cutoffs for overweight in those populations.

## 4.3. Methods

### *4.3.1. Study population*

We used three data sets from recent, representative surveys: the China Health and Nutrition Survey in 2004 (CHNS; n = 7562), the Indonesian Family Life Survey in 2000 (IFLS; n = 18502), and the Vietnam National Health Survey in 2002 (VNHS; n = 77758). The surveys have been described elsewhere (Popkin, Paeratakul et al. 1995; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004; Tuan, Tuong et al. 2008). To summary, the CHNS in 2004 was a part of an ongoing study established in the late 1980s in 9 China provinces that vary substantially in geography, economic development, public resources, and health indicators. The sample represented about 50% of the Chinese population. The IFLS in 2000 was a part of an ongoing longitudinal survey established in the early 1990s in 13 Indonesia provinces. The sample represented about 83% of the Indonesian population. The VNHS in 2002 was the largest, nationally representative health survey ever conducted in all 61 Vietnam provinces. Survey instructions, data sets, and questionnaires may be downloaded from the Web sites of the CHNS (http://www.cpc.unc.edu/china), the IFLS (http://www.rand.org/labor/FLS/IFLS/), and the Vietnam Ministry of Health (http://www.moh.gov.vn ).

We only included participants who were 18- to 65-y-old men, nonpregnant or nonlactating women at the time of survey, whom measurements of weight, height, or blood pressure were complete or plausible (e.g., BMI of 15–35 kg/m$^2$; weight of 30–150 kg; height of 130–90 cm; and the difference between systolic and diastolic blood pressures > 10 mmHg). We only included 18- to 65-y-old adults, including nonpregnant and nonlactating women because a teenager, an older person, or a pregnant or lactating woman requires different BMI cutoffs (WHO expert committee 1995). The exclusion of participants with extreme or implausible values of anthropometric measures or blood pressures helped to increase our estimate precision without changing the overall results.

#### *4.3.2. Study design*

Blood pressure measurements were taken in a seated position and on the right arm by trained health workers who followed a standardized procedure using regularly calibrated mercury sphygmomanometers (CHNS), Omron digital devices (IFLS), or aneroid manometers (VNHS) with appropriate-sized cuffs. In the CHNS and VNHS, systolic blood pressure was measured at the first appearance of a pulse sound (Korotkoff phase 1) and diastolic blood pressure at the disappearance of the pulse sound (Korotkoff phase 5); three measurements of systolic or diastolic blood pressure were averaged to reduce the effect of measurement errors. In the IFLS, systolic and diastolic blood pressures were obtained from the digital device (Popkin, Paeratakul et al. 1995; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004). Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed by a doctor (Chobanian, Bakris et al. 2003). We did not include the use of an antihypertensive medication to define hypertension, because (a) in the VNHS and IFLS, information about the treatment was not available and (b) in the CHNS, only a small proportion of Chinese adults was diagnosed (< 7%) or treated (< 5%) with any antihypertensive medications and none used the medications without being diagnosed by a doctor. Moreover, sensitivity analysis showed that incorporating these measures produced similar findings but with a smaller sample size.

BMI ($kg/m^2$) was calculated based on weight and height, which were measured by trained health workers who followed standardized procedures and used regularly calibrated equipment. The CHNS used SECA 880 scales and SECA 206 wall-mounted metal tapes; the IFLS and VNHS used SECA 890 scales and Shorr measuring boards (Popkin, Paeratakul et al. 1995; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004). Covariates such as age, sex, smoking habits, alcohol consumption, and place of residence were collected by direct interviews.

#### *4.3.3. Statistical methods*

We used Poisson regression models to examine the association between BMI and hypertension. Potential confounding factors at baseline, such as age (centered at 40 y), sex, smoking habits (dichotomized to never-smoker or ever-smoker), alcohol consumption (dichotomized to current drinker or nondrinker), and place of residence (urban or rural) were taken into account in regression models. A covariate was considered as an effect-measure modifier if its interaction term with BMI in regression models had a $P$-value < 0.15 (chi-square test) or as a confounder if it caused a change in incidence ratios of >10%. Based on these criteria, the most reduced model had age as an effect-measure modifier (the association between BMI and hypertension was stronger in the younger participants) and sex as confounding factor. We purposely stratified our analyses by sex to make them comparable with other studies. To estimate the differences in BMI and hypertension association, we compared prevalence and prevalence ratio (PR), which were obtained from crude, age-adjusted or age-specific models, among difference ethnicities.

To evaluate an optimal BMI cutoff, we computed and searched for the shortest distance on the sex-specific ROC curve, estimated at each one-half unit of BMI. A distance on the ROC curve is equal to $\sqrt{(1-sensitivity)^2+(1-specificity)^2}$ (Wildman, Gu et al. 2004). Given the large sample sizes, in each ethnicity, we performed stratified analyses by age and sex groups. We used 2-tail independent *t* tests to compare 2 means and chi-square tests to compare different levels or trends of categorized variables. We conducted all analyses using Stata software version 9.2 (Stata Inc., TX, USA).

#### *4.3.4. Role of the funding sources and ethical consideration*

The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The sponsors were not involved in the study design, the collection, analysis, or interpretation of data, the writing or submission of the manuscript for publication. The Institutional Review Boards (IRB) of the School of Public Health, University of North Carolina at Chapel Hill reviewed and approved the study.

## 4.4. Results

The prevalence of hypertension in Chinese, Indonesian, and Vietnamese women was 16.6, 26.9, and 11.7%, respectively. Indonesian women had the highest mean diastolic and systolic blood pressures compared to Chinese and Vietnamese women. The prevalence of hypertension in Chinese, Indonesian, and Vietnamese men was 22.9, 24.8, and 14.4%, respectively. Indonesian men had the highest mean diastolic and systolic blood pressures compared to Chinese and Vietnamese men (**Table 4.1**).

The mean BMI of Chinese, Indonesian, and Vietnamese women was 23.1, 22.4, and 20.4 kg/m$^2$, respectively. The BMI distributions were skewed to the right (Skewness values of 0.5–1.0) (**Fig. 4.1***A*). The mean BMI of Chinese, Indonesian, and Vietnamese men was 23.1, 21.2, and 20.2 kg/m$^2$, respectively. The BMI distributions in men were also skewed to the right (Skewness values of 0.5–1.0) (Fig. 4.1*B*). Chinese women and men had higher prevalence of overweight (BMI $\geq$ 25 kg/m$^2$) compared to Indonesian or Vietnamese women and men, respectively (Table 4.1).

For each ethnicity, there was a significant trend of increased sex-specific prevalence of hypertension with an increase in BMI ($P$ for trend < 0.001). At each BMI level, sex-specific prevalence of hypertension was highest in Indonesian adults compared to those of Chinese and Vietnamese adults ($P < 0.05$ at almost all BMI levels) (**Fig. 4.2** *A*, *B*). The predicted prevalence of hypertension (in a hypothesized population where all participants were 40 y-olds) remained highest in Indonesian adults at all BMI levels compared to those of Chinese and Vietnamese adults ($P < 0.05$ for all) (Fig. 4.2 *C*, *D*).

On average, each unit increase in BMI was associated with an increase of 18, 8, and 16% (women); 14, 12, and 14% (men) in PR for hypertension among Chinese, Indonesian, and Vietnamese adults, respectively (crude models). In women, there was a significant trend of increased ethnic-specific PR with an increase in BMI (*P* for trend < 0.001) in both crude and age-adjusted models. PR was highest in Chinese women and lowest in Indonesian women (**Fig. 4.3** *A,B*). There was also a significant trend of increased sex-specific PR with an increase in BMI in Chinese, Indonesian, and Vietnamese men (*P* for trend < 0.001). PR was comparable in men, except among the obese (BMI ≥ 30 kg/m$^2$) in age-adjusted model (**Fig. 4.3** *C,D*).

Based on the shortest distance on the ROC curve (corresponding to the largest combination of sensitivity and specificity) optimal BMI cutoffs were 23.5, 22.0, and 20.5 kg/m$^2$ in Chinese, Indonesian, and Vietnamese adults, respectively. A BMI level of 25 kg/m$^2$ provided lower sensitivities, especially in Vietnamese and Indonesian adults (**Fig. 4.4** *A*). Similar trends were found in women (Fig. 4.4 *B*) and men (Fig. 4.4 *C*). Based on the ROC curve approach, optimal BMI cutoffs in Chinese adults were larger than those in Indonesian (about 1.5 units) and Vietnamese (about 3 units) adults. BMI cutoffs were about 0.5–1.0 unit higher in women compared to men and in the older (41- to 65-y-old) compared to the younger (18- to 40-y-old) participants. Stratified and overall analyses showed an optimal BMI cutoff of 23–24, 21–22.5, and 20.5–21 kg/m$^2$ for Chinese, Indonesian, and Vietnamese adults, respectively. AUC values for the prediction of hypertension by BMI, which ranged from 0.6 to 0.7, were highest in Chinese in both overall and stratified analyses (**Table 4.2**).

### 4.5. Discussion

In this study, we found ethnic differences in the association between BMI and hypertension in Chinese, Indonesian, and Vietnamese adults. The differences could be explained by the variation in the body fat. For example, at the same age, sex, and BMI, Indonesians have more body fat than Chinese adults (Deurenberg, Yap et al. 1998). With an assumption that total visceral fat is linearly associated with total body fat, Indonesian adults would have more visceral fat at a given BMI, and thus have a higher cardiovascular risk (e.g., hypertension) compared to Chinese adults (Kaplan 2006; Sniderman, Bhopal et al. 2007). Because there are no similar data on Vietnamese body fat distribution by BMI levels, we are not able to use this theory to explain the difference in prevalence of hypertension between Indonesian and Vietnamese adults.

Differences in genes and gene-environment interactions would be another potential explanation for the differences in the BMI specific prevalence of hypertension. Findings from gene-family environment, twin, and migration studies showed the roles of both genetic, ethnic and environmental factors in the development of chronic diseases (Luft 2001; Cui, Hopper et al. 2002; Misra and Ganda 2007; Razak, Anand et al. 2007). Chinese and Vietnamese populations are expected to share more genetic background compared to the Indonesian population because they evolved from a branch of *Homo sapiens* that differed from the branch that evolved into the Indonesians (Maca-Meyer, Gonzalez et al. 2001; Macaulay, Hill et al. 2005). The different genetic background interacts differently with diverse environmental factors relating to hypertension such as dietary intakes, physical activity levels, food habits, cultures, religions, demographic characteristics, and socio-economic status (Bell, Adair et al. 2004; Merlo, Asplund et al. 2004), which lead to different prevalence of hypertension. In-depth analyses that take into account genetic, individual, and environmental factors are still needed to explore the complex association between BMI and related chronic diseases.

The variation in blood pressure measurements is unlikely to alter the prevalence of hypertension. First, these surveys (CHNS, IFLS, and VNHS) followed a standardized protocol in measuring blood pressures (Popkin, Paeratakul et al. 1995; Chobanian, Bakris et al. 2003; Ministry of Health - General Statistical Office 2003; Strauss, Beegle et al. 2004). Second, the regularly calibrated sphygmomanometers used in these surveys are in the list of recommended equipment (O'Brien, Waeber et al. 2001). Finally, the rounding error in measuring blood pressure was not an issue in any survey (in the CHNS and VNHS, we used the mean three measurements of blood pressure; and in the IFLS we used non-rounded values from digital sphygmomanometers). However, because the first measurement of blood pressure is usually higher than the next measurements (Chobanian, Bakris et al. 2003), blood pressures would be systematically elevated in IFLS compared to the mean three measurements (if they had been ideally collected). Compared to the mean three measurements, the first measurement caused a negligible overestimation of systolic and diastolic blood pressures (< 0.15 and < 0.05 mmHg in CHNS; and < 1.25 and < 0.75 mmHg in VNHS). To explore further the magnitude of the overestimation in blood pressure (in IFLS), we conducted a sensitivity analysis with a subtraction of 1.5 and 1.0 mmHg from systolic and diastolic blood pressures, respectively. Although there was a 2% decrease in prevalence of hypertension, all other predictions (e.g., PR, AUC, BMI cutoffs) and overall conclusions were unchanged (**Supplementary Tables 4.1 and 4.2**).

In this study, we found ethnic differences in optimal BMI cutoffs. The differences in optimal BMI cutoffs would be results of different association between BMI and hypertension that have been presented earlier. In addition, the sensitivity and specificity of a screening test (in this case, a BMI level to predict hypertension) depend on both distribution of exposure, outcome, and other covariates (e.g., factors at individual or environmental levels). For example, if we hold other variables unchanged and add a constant to BMI, the optimal BMI level will increase with the added value. This mathematic imputation shows that BMI distribution affects optimal BMI level. Our finding that a higher BMI cutoff is found in a population with a higher mean BMI is consistent with other studies (Bei-Fan 2002; Lin, Lee et al. 2002; Mohan, Deepa et al. 2007).

However, the difference in mean BMI could not explain all of the differences in optimal BMI cutoffs. An increase in cardiovascular risk, which is associated with an increase in BMI, allows us to detect elevated a cardiovascular risk at a lower BMI, and thus, leads to a decrease in optimal BMI cutoff. In combination with other complex changes or differences in environmental factors, although we knew the difference in mean BMI of given populations, we are not able to predict the difference in optimal BMI cutoff. For example, in our samples, the differences in the mean BMI in Chinese, Indonesian, and Vietnamese adults were not proportionally related to the variations in optimal BMI cutoffs. Chinese men in our population had a higher mean BMI, but a smaller optimal BMI cutoff compared to the finding from Bei-Fan et al. (Bei-Fan 2002); and Chinese women in our population had the same mean BMI, but a higher optimal BMI cutoff compared to the finding from Mohan et al. (Mohan, Deepa et al. 2007). Another counterexample is that South Asian Canadians had a higher mean BMI, but a lower BMI cutoff based on lipid factors compared to Chinese Canadians (Razak, Anand et al. 2007). Because the differential changes in mean BMI and in prevalence of hypertension, are probably clustered by groups of ethnicities, genetic factors, age, sex, lifestyles, and socio-economic status, the ethnic or country specific BMI cutoff should be understood as the combination of all factors.

The recommendation of lowering BMI cutoffs for Chinese, Indonesian, and Vietnamese is consistent with results from large-scale cross-sectional studies in Asian populations (Bei-Fan 2002; Lin, Lee et al. 2002; Wildman, Gu et al. 2004; Mohan, Deepa et al. 2007; Huxley, James et al. 2008). In those studies, a BMI cutoff of 22–24 $kg/m^2$ was associated with an increase in prevalence of hypertension, diabetes mellitus, dyslipidemia, and cardiovascular diseases. The explanations for the ethnic differences have been presented elsewhere (Misra 2003; WHO expert consultation 2004; Nguyen, Adair et al. 2008). To summary, first, Asian ethnicities tend to have a higher total body fat (Wang, Thornton et al. 1994; Deurenberg, Deurenberg-Yap et al. 2002), a greater abdominal and visceral fat (Park, Allison et al. 2001; Lear, Humphries et al. 2007) at a given BMI compared to other races and ethnicities, which lead to increased cardiovascular risk (Kaplan 2006; Sniderman, Bhopal et al. 2007). Second, differences in gene, environmental, and gene-environment interactions (Carretero and Oparil 2000; Luft 2001; Maca-Meyer, Gonzalez et al. 2001; Cui, Hopper et al. 2002; Bell, Adair et al. 2004; Merlo, Asplund et al. 2004; Kaplan 2006) lead to the ethnic variation in phenotype of blood pressure. Third, there is also speculation that any insults during fetal development and infancy might have also resulted in the elevated risks (Barker 2002; Williams and Poulton 2002; Adair and Cole 2003; Demerath, Cameron et al. 2004; Singhal and Lucas 2004). In addition, Asian populations are younger and have lower mean BMI compared to Western populations, which both lead to the decrease in optimal cutoffs.

Our findings were based on large, recent, representative samples from China, Indonesia, and Vietnam, which ensured the generalizability of the findings to respective populations. However, similar to other cross-sectional studies, we did not ensure if the exposure to a higher BMI had preceded hypertension outcome. Compared to BMI optimal cutoffs for overweight for Chinese adults obtained from the CHNS 2000 – 2004 cohort (Nguyen, Adair et al. 2008), these optimal BMI cutoffs (from the CHNS cross-sectional sample in 2004) were 0.5–1 unit larger. Given almost all studies aiming at determining optimal BMI cutoffs for Asians were based on cross-sectional samples, a certain adjustment for the cross-sectional cutoffs might be needed.

In conclusion, although there are ethnic differences in the association between BMI and hypertension as well as variations in optimal BMI cutoffs for overweight in Chinese, Indonesian, and Vietnamese adults, an optimal BMI cutoffs $< 25$ kg/m$^2$ maybe more appropriate for the East and Southeast Asian populations. A lower BMI cutoff is important in developing countries because in those countries, overweight and related chronic diseases are becoming emerging problems (Popkin 2006) and are not adequately prevented, diagnosed, and managed (Mendis, Abegunde et al. 2004). Country-specific or even country-, sex-, age-specific BMI cutoffs for overweight would be needed to identify people at high risk of cardiovascular diseases and to reduce health and economic burdens of both overweight and chronic diseases.

**Table 4.1.** Characteristics of 18- to 65-y-old participants by sex and ethnic groups[1]

| | Women | | | | | | Men | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Chinese (n =3913) | | Indonesian (n = 8888) | | Vietnamese (n = 39711) | | Chinese (n = 3649) | | Indonesian (n = 9614) | | Vietnamese (n = 38047) | |
| | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI |
| Age, *y* | 44.0 | (43.6–44.4) | 39.1* | (38.8–39.4) | 38.6*,† | (38.5–38.8) | 43.7 | (43.3–44.1) | 37.6* | (37.3–37.8) | 37.1*,† | (37.0–37.2) |
| Hypertension[2], *%* | 16.6 | (15.4–17.8) | 26.9* | (25.9–27.9) | 11.7*,† | (11.3–12.1) | 22.9 | (21.5–24.2) | 24.8 | (23.8–25.8) | 14.4*,† | (13.9–14.9) |
| Systolic BP, *mm Hg* | 117.8 | (117.2–118.3) | 124.1* | (123.6–124.7) | 116.2*,† | (115.9–116.4) | 122.1 | (121.6–122.6) | 125.8* | (125.4–126.2) | 120.0*,† | (119.8–120.3) |
| Diastolic BP, *mm Hg* | 76.7 | (76.4–77.1) | 80.4* | (80.1–80.6) | 73.4*,† | (73.3–73.6) | 80.1 | (79.7–80.4) | 80.5 | (80.3–80.8) | 76.1*,† | (75.9–76.3) |
| BMI, $kg/m^2$ | 23.1 | (23.0–23.2) | 22.4* | (22.3–22.5) | 20.4*,† | (20.3–20.4) | 23.1 | (23.0–23.2) | 21.2* | (21.2–21.3) | 20.2*,† | (20.2–20.3) |
| 15–18.5 $kg/m^2$, *%* | 6.0 | (5.3–6.8) | 14.3* | (13.5–15.1) | 25.9*,† | (25.3–26.5) | 4.9 | (4.2–5.6) | 16.6* | (15.8–17.5) | 22.7*,† | (22.2–23.3) |
| 18.5–22.9 $kg/m^2$, *%* | 47.2 | (45.6–48.8) | 46.6 | (45.5–47.8) | 58.7*,† | (58.1–59.3) | 48.2 | (46.6–49.8) | 59.6* | (58.5–60.7) | 65.7*,† | (65.1–66.3) |
| 23–24.9 $kg/m^2$, *%* | 19.8 | (18.6–21.1) | 15.5* | (14.7–16.3) | 9.2*,† | (8.9–9.5) | 21.7 | (20.3–23.0) | 12.0* | (11.3–12.8) | 7.4*,† | (7.1–7.7) |
| 25–29.9 $kg/m^2$, *%* | 23.4 | (22.1–24.8) | 19.1* | (18.2–20.0) | 5.7*,† | (5.5–6.0) | 22.4 | (21.1–23.8) | 10.5* | (9.8–11.2) | 3.9*,† | (3.7–4.2) |
| 30–35 $kg/m^2$, *%* | 3.6 | (3.0–4.1) | 4.5 | (4.0–4.9) | 0.5*,† | (0.4–0.5) | 2.8 | (2.3–3.3) | 1.2* | (1.0–1.4) | 0.2*,† | (0.1–0.2) |
| Weight, *kg* | 56.4 | (56.1–56.7) | 50.7* | (50.4–50.9) | 47.3*,† | (47.2–47.5) | 64.5 | (64.2–64.9) | 55.7* | (55.5–55.9) | 53.7*,† | (53.5–53.8) |
| Height, *cm* | 156.2 | (156.0–156.4) | 150.2* | (150.0–150.3) | 152.4*,† | (152.3–152.5) | 167.1 | (166.8–167.3) | 161.8* | (161.6–161.9) | 162.8*,† | (162.7–162.9) |
| Smoking status | | | | | | | | | | | | |
| Former smoker, *%* | 0.1 | (0.0–0.2) | 0.6* | (0.4–0.8) | 0.5* | (0.4–0.6) | 5.6 | (4.8–6.3) | 5.0 | (4.5–5.5) | 13.0*,† | (12.5–13.5) |
| Current smoker, *%* | 3.1 | (2.5–3.6) | 5.1* | (4.6–5.6) | 1.9*,† | (1.7–2.1) | 58.9 | (57.3–60.5) | 69.0* | (68.0–70.0) | 65.0*,† | (64.3–65.7) |
| Alcohol drinker, *%* | 8.9 | (8.0–9.8) | - | | 1.9* | (1.7–2.1) | 62.3 | (60.7–63.8) | - | | 53.3*,† | (52.4–54.1) |
| Urban residence, *%* | 34.0 | (32.5–35.4) | 45.5* | (44.4–46.7) | 26.5*,† | (26.0–27.1) | 34.1 | (32.6–35.6) | 44.9* | (43.9–46.0) | 25.8*,† | (25.2–26.5) |

BP, Blood pressure; Est, estimate.
[1] Values are means or percentages with 95% CI; the samples included participants with plausible anthropometric indices (e.g. BMI <15 or >35 $kg/m^2$). [2] Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed a doctor. * Different from Chinese, $P < 0.05$; † Different from Indonesian, $P < 0.05$; 2-tail independent *t* test for continuous variables or chi-square test for categorized variables.

**Table 4.2.** Optimal body mass index cutoffs for overweight by sex and age groups[1]

| | Chinese | | | | | Indonesian | | | | | Vietnamese | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Cutoffs | Sen | Spe | AUC | n | Cutoffs | Sen | Spe | AUC | n | Cutoffs | Sen | Spe | AUC |
| Both sexes | | | | | | | | | | | | | | | |
| All age | 7562 | 23.5 | 0.63 | 0.64 | 0.68 | 18502 | 22 | 0.55 | 0.65 | 0.63 | 77758 | 20.5 | 0.57 | 0.61 | 0.62 |
| 18–40 y | 2843 | 23 | 0.63 | 0.66 | 0.68 | 11373 | 21.5 | 0.57 | 0.61 | 0.63 | 44646 | 20.5 | 0.56 | 0.65 | 0.64 |
| 41–65 y | 4719 | 24 | 0.59 | 0.65 | 0.66 | 7129 | 22.5 | 0.54 | 0.64 | 0.61 | 33112 | 21 | 0.52 | 0.62 | 0.59 |
| Women | | | | | | | | | | | | | | | |
| All age | 3913 | *24* | 0.63 | 0.69 | 0.70 | 8888 | 22.5 | 0.57 | 0.61 | 0.62 | 39711 | 21 | 0.57 | 0.66 | 0.64 |
| 18–40 y | 1451 | 23 | 0.66 | 0.69 | 0.68 | 5200 | 22.5 | 0.56 | 0.64 | 0.63 | 21766 | 20.5 | 0.57 | 0.64 | 0.64 |
| 41–65 y | 2462 | 24 | 0.64 | 0.63 | 0.68 | 3688 | 22.5 | 0.58 | 0.56 | 0.59 | 17945 | 21 | 0.58 | 0.59 | 0.60 |
| Men | | | | | | | | | | | | | | | |
| All age | 3649 | 23.5 | 0.61 | 0.65 | 0.67 | 9614 | 21.5 | 0.54 | 0.66 | 0.64 | 38047 | 20.5 | 0.53 | 0.63 | 0.60 |
| 18–40 y | 1392 | 23.5 | 0.58 | 0.67 | 0.67 | 6173 | 21 | 0.57 | 0.61 | 0.64 | 22880 | 20.5 | 0.55 | 0.65 | 0.63 |
| 41–65 y | 2257 | 23.5 | 0.61 | 0.63 | 0.66 | 3441 | 22 | 0.54 | 0.67 | 0.63 | 15167 | 20.5 | 0.52 | 0.58 | 0.58 |

AUC, Area Under the Curve; Sen, Sensitivity; Spe, specificity.
[1] AUC values range from 0.5 (no prediction) to 1.0 (perfect prediction).

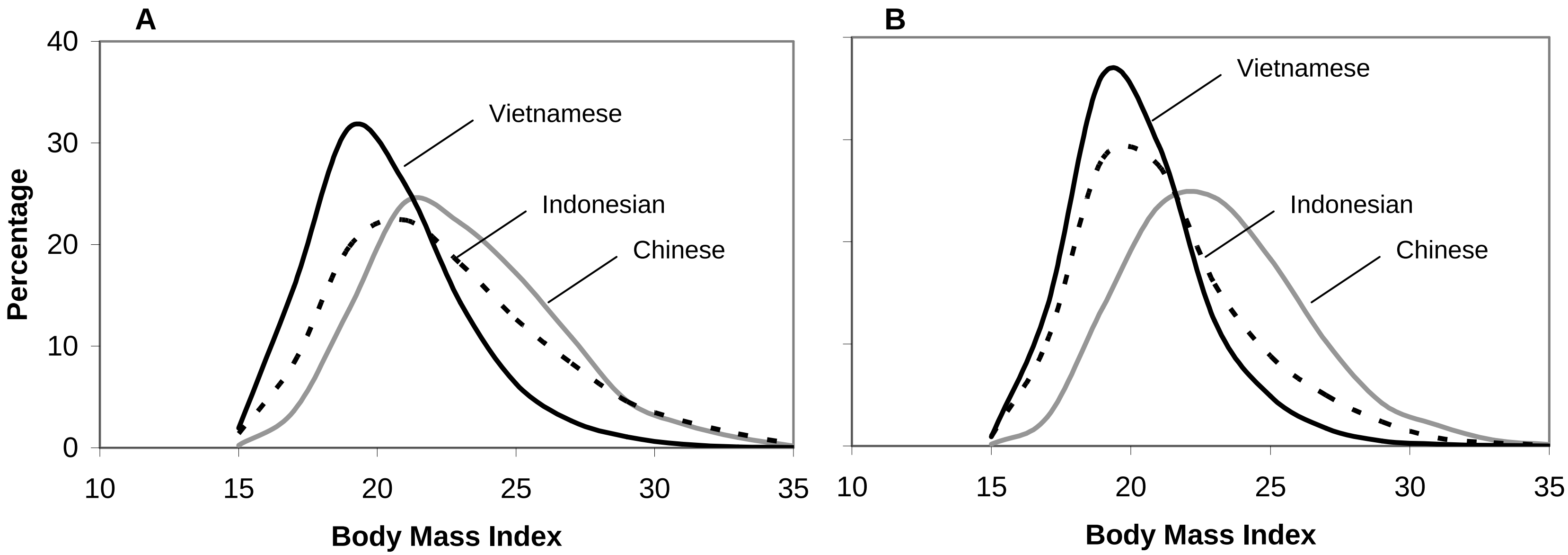


**Figure 4.1.** Distribution of body mass index levels in women (*A*) and men (*B*)

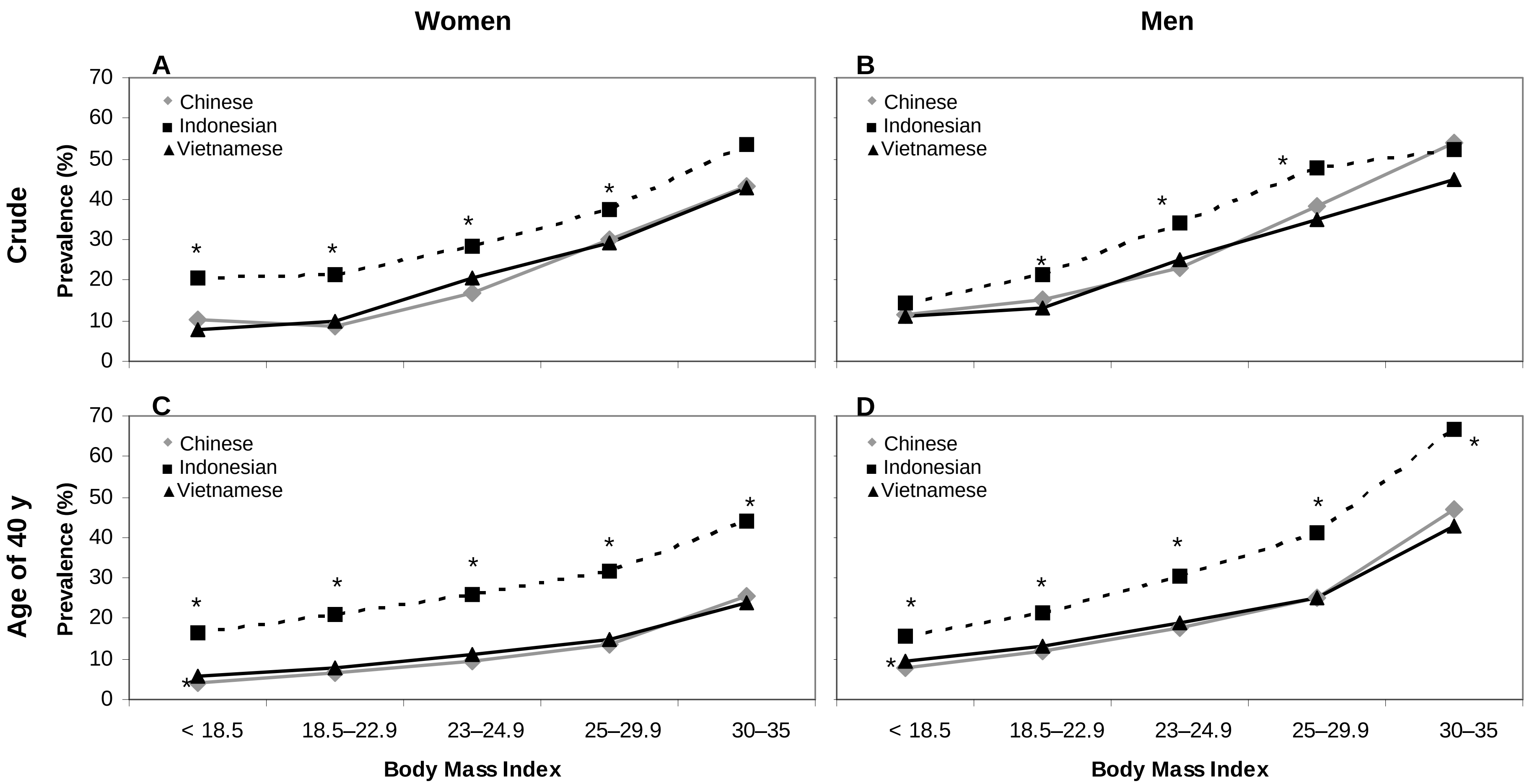


**Figure 4.2.** Prevalence of hypertension by body mass index levels in Chinese, Indonesian, and Vietnamese. (*A*) Crude prevalence in women, (*B*) Crude prevalence in women, (*C*) at age of 40 y in women, and (*D*) at age of 40 y in men.

* $P < 0.05$ compared to Chinese, chi-square test; $P$ for trend < 0.05 for all

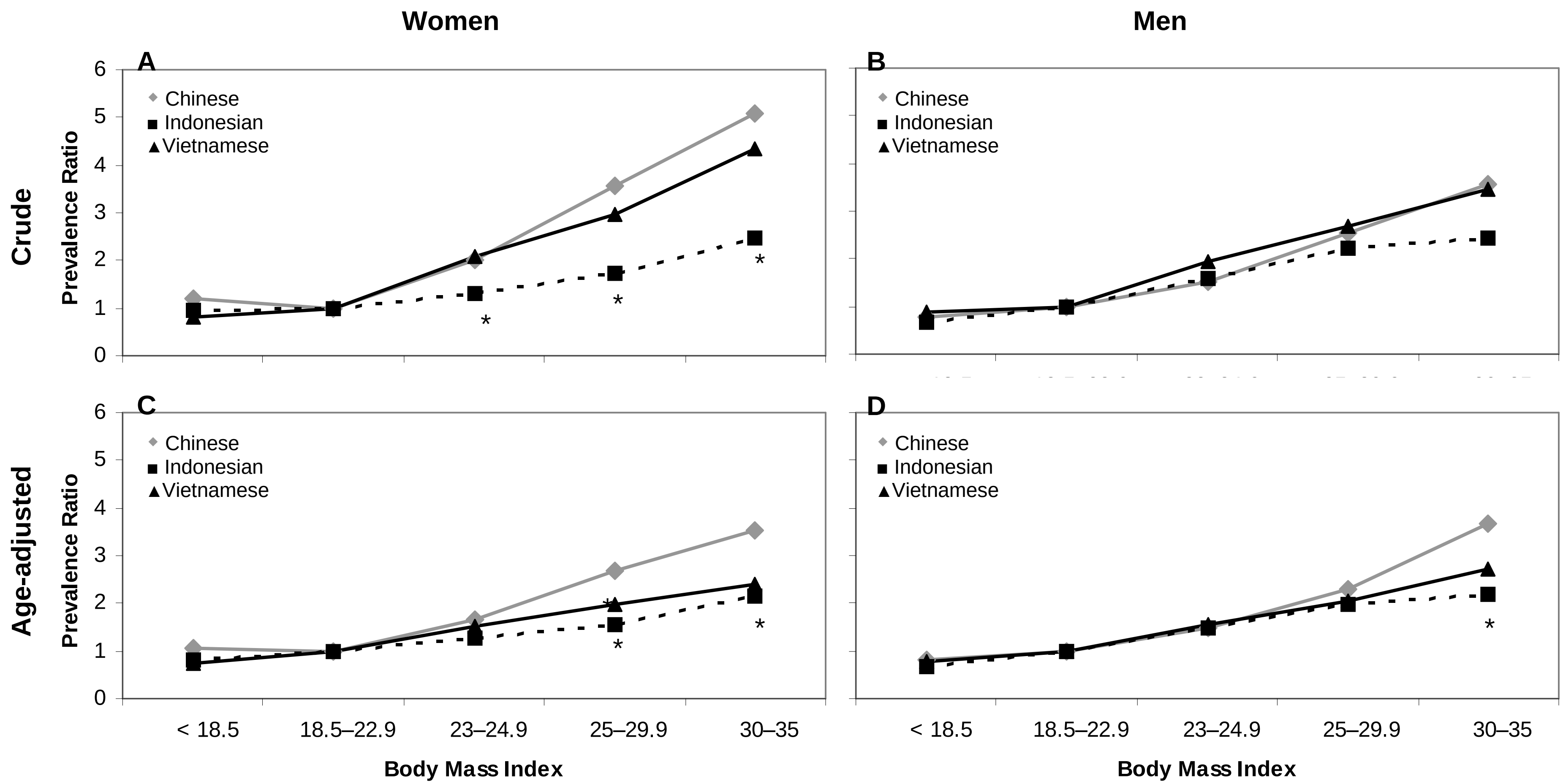


**Figure 4.3.** Prevalence ratio of hypertension by body mass index levels in Chinese, Indonesian, and Vietnamese. (*A*) Crude in women, (*B*) Crude in women, (*C*) age-adjusted in women, and (*D*) age-adjusted in men.
BMI of 18.5–22.9 kg/m$^2$ was reference group. * $P < 0.05$ compared to Chinese, chi-square test; $P$ for trend < 0.05 for all

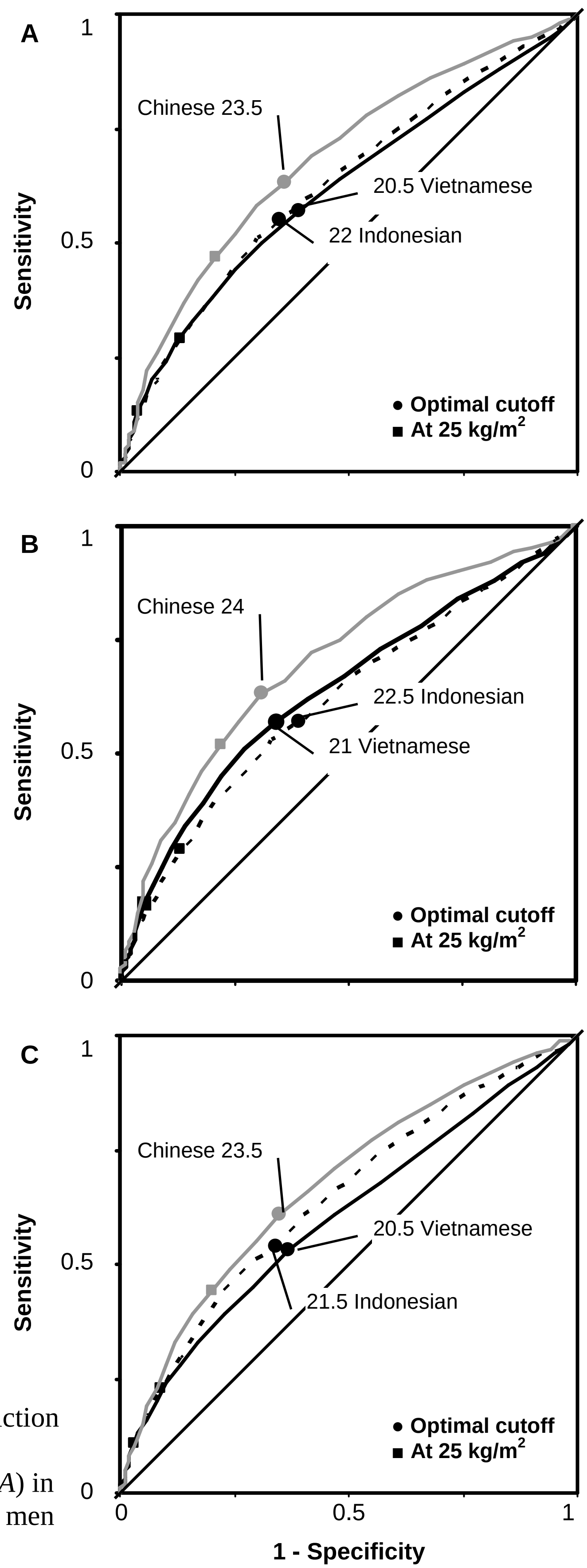


**Figure 4.4.** ROC curves for the prediction of hypertension by BMI in Chinese, Indonesian, and Vietnamese adults. (*A*) in both sexes; (*B*) in women; and (*C*) in men

**Supplementary Table 4.1.** Prevalence and prevalence ratio of hypertension: comparison between the measured blood pressure and adjusted blood pressures the sample of Indonesian adults[1,2]

| | Women (n = 8888) | | | | Men (n = 9614) | | | |
|---|---|---|---|---|---|---|---|---|
| | Based on measured blood pressures | | Based on adjusted blood pressures | | Based on measured blood pressures | | Based on adjusted blood pressures | |
| | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI | Est. | 95%CI |
| **Prevalence** | | | | | | | | |
| **Crude** | 26.9 | (25.9–27.9) | 24.6* | (23.6–25.6) | 24.8 | (23.8–25.8) | 22.1 | (21.2–23.0) |
| BMI ($kg/m^2$) levels | | | | | | | | |
| < 18.5, % | 20.7 | (18.1–23.2) | 19.3 | (16.8–21.8) | 14.5 | (12.6–16.4) | 12.6 | (10.8–14.4) |
| 18.5–22.9, % | 21.5 | (20.1–22.9) | 19.2 | (17.9–20.6) | 21.3 | (20.1–22.5) | 18.5 | (17.4–19.7) |
| 23–24.9, % | 28.4 | (25.7–31.0) | 25.3 | (22.8–27.9) | 34.0 | (31.0–37.1) | 30.6 | (27.6–33.6) |
| 25–29.9, % | 37.4 | (34.8–39.9) | 35.8 | (33.3–38.4) | 47.6 | (44.1–51.0) | 44.4 | (41.0–47.9) |
| 30–35, % | 53.4 | (47.9–58.8) | 47.3 | (41.9–52.8) | 52.1 | (41.8–62.5) | 50.5 | (40.1–60.8) |
| **Age of 40 y** | | | | | | | | |
| BMI ($kg/m^2$) levels | | | | | | | | |
| < 18.5, % | 16.7 | (15.6–17.8) | 14.6 | (13.6–15.7) | 15.7 | (14.8–16.8) | 13.4 | (12.5–14.4) |
| 18.5–22.9, % | 20.9 | (19.9–21.9) | 18.5* | (17.5–19.5) | 21.5 | (20.6–22.5) | 18.7* | (17.8–19.6) |
| 23–24.9, % | 25.9 | (24.8–27.0) | 23.0* | (22.0–24.1) | 30.4 | (29.2–31.6) | 27.0* | (25.9–28.2) |
| 25–29.9, % | 31.8 | (30.3–33.3) | 28.5* | (27.1–30.0) | 41.3 | (39.2–43.5) | 37.4* | (35.4–39.6) |
| 30–35, % | 43.9 | (40.7–47.4) | 39.9 | (36.8–43.2) | 66.7 | (61.1–72.9) | 62.4 | (56.8–68.5) |
| **Prevalence Ratio** | | | | | | | | |
| **Crude** | **1.08** | **(1.07–1.08)** | 1.08 | (1.07–1.09) | **1.12** | **(1.11–1.13)** | 1.13 | (1.12–1.14) |
| BMI ($kg/m^2$) levels | | | | | | | | |
| < 18.5, % | 0.96 | (0.84–1.10) | 1.00 | (0.87–1.16) | 0.68 | (0.59–0.79) | 0.68 | (0.58–0.79) |
| **18.5–22.9**, % | 1 | | 1 | | 1 | | 1 | |
| 23–24.9, % | 1.32 | (1.18–1.48) | 1.32 | (1.16–1.49) | 1.60 | (1.44–1.78) | 1.65 | (1.47–1.85) |
| 25–29.9, % | 1.74 | (1.58–1.91) | 1.86 | (1.69–2.06) | 2.24 | (2.04–2.45) | 2.40 | (2.17–2.64) |
| 30–35, % | 2.48 | (2.20–2.80) | 2.46 | (2.15–2.81) | 2.45 | (2.00–3.01) | 2.72 | (2.20–3.37) |
| **Age-adjusted** | **1.07** | **(1.06–1.08)** | 1.07 | (1.06–1.08) | **1.11** | **(1.10–1.12)** | 1.12 | (1.10–1.13) |
| BMI ($kg/m^2$) levels | | | | | | | | |
| < 18.5, % | 0.82 | (0.72–0.93) | 0.83 | (0.73–0.96) | 0.66 | (0.58–0.76) | 0.66 | (0.56–0.76) |
| **18.5–22.9**, % | 1 | | 1 | | 1 | | 1 | |
| 23–24.9, % | 1.27 | (1.14–1.42) | 1.27 | (1.13–1.43) | 1.47 | (1.33–1.63) | 1.51 | (1.35–1.68) |
| 25–29.9, % | 1.56 | (1.42–1.70) | 1.66 | (1.51–1.82) | 1.97 | (1.80–2.15) | 2.09 | (1.89–2.30) |
| 30–35, % | 2.15 | (1.91–2.42) | 2.12 | (1.86–2.41) | 2.19 | (1.80–2.66) | 2.40 | (1.96–2.94) |

[1] Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed a doctor. [2] Adjusted blood pressures are equal measured systolic blood pressure minus 1.5 mmHg and diastolic blood pressure minus 1.0 mmHg;
[*] $P < 0.05$ compared to measured blood pressure

**Supplementary Table 4.2.** Body mass index cutoffs for overweight corresponding to increased prevalence of hypertension by gender and age groups: comparison between the measured blood pressure and adjusted blood pressure the sample of Indonesian adults[1,2]

| | | Based on measured blood pressure | | | | Based on adjusted blood pressure | | | |
|---|---|---|---|---|---|---|---|---|---|
| | n | **Cutoffs** | Sen | Spe | AUC | **Cutoffs** | Sen | Spe | AUC |
| Both sexes | | | | | | | | | |
| All age | 18502 | **22** | 0.55 | 0.65 | 0.63 | **22** | 0.56 | 0.64 | 0.63 |
| 18–40 y | 11373 | **21.5** | 0.57 | 0.61 | 0.63 | **21.5** | 0.58 | 0.61 | 0.64 |
| 41–65 y | 7129 | **22.5** | 0.54 | 0.64 | 0.61 | **22.5** | 0.55 | 0.64 | 0.61 |
| Women | | | | | | | | | |
| All age | 8888 | **22.5** | 0.57 | 0.61 | 0.62 | **22.5** | 0.58 | 0.61 | 0.62 |
| 18–40 y | 5200 | **22.5** | 0.56 | 0.64 | 0.63 | **22.5** | 0.57 | 0.64 | 0.64 |
| 41–65 y | 3688 | **22.5** | 0.58 | 0.56 | 0.59 | **22.5** | 0.59 | 0.56 | 0.59 |
| Men | | | | | | | | | |
| All age | 9614 | **21.5** | 0.54 | 0.66 | 0.64 | **21.5** | 0.56 | 0.66 | 0.64 |
| 18–40 y | 6173 | **21** | 0.57 | 0.61 | 0.64 | **21** | 0.58 | 0.61 | 0.64 |
| 41–65 y | 3441 | **22** | 0.54 | 0.67 | 0.63 | **22** | 0.55 | 0.67 | 0.63 |

[1] Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed a doctor. [2] Adjusted blood pressures are equal measured systolic blood pressure minus 1.5 mmHg and diastolic blood pressure minus 1.0 mmHg;

# CHAPTER 5. OPTIMAL CUTOFF VALUES FOR OVERWEIGHT: USING BODY MASS INDEX TO PREDICT INCIDENCE OF HYPERTENSION IN 18–65-YEAR-OLD CHINESE ADULTS

## 5.1. Abstract

Studies aimed at identifying body mass index (BMI) cutoffs representing increased diseased risk for Asians are typically based on cross sectional studies. This study determines an optimal BMI cutoff for overweight that represents elevated incidence of hypertension in Chinese adults with data from the China Health and Nutrition Survey 2000–2004 prospective cohort. Cumulative incidence was calculated by dividing new cases of hypertension over the study period by the total at-risk population, aged 18–65 years, in 2000. Sex-specific receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of BMI as a predictor of hypertension incidence. Four-year cumulative incidences of hypertension (13% and 19% for women and men, respectively) were significantly ($P <$ 0.005) related to the increase in BMI. The crude area under the curves (AUC) were 0.62 (95% CI: 0.59–0.65) and 0.62 (95% CI: 0.58–0.65) for men and women, respectively; the age-adjusted AUC were 0.68 (95% CI: 0.65–0.70) and 0.71 (95% CI: 0.68–0.74) for men and women, respectively. A BMI of 23.5 kg/m$^2$ for women and 22.5 kg/m$^2$ for men provided highest sensitivity and specificity (60%). The finding was consistent in different age groups. A BMI level of 25 kg/m$^2$ provided lower sensitivities (36% for women and 29% for men) with higher specificities (80% for women and 85% for men). Our study supported the

hypothesis that the BMI cutoff to define overweight should be lower in Chinese than in Western populations.

## 5.2. Introduction

Increased prevalence, attributable dea[illegible]d economic burdens of overweight and non-communicable diseases are emerging problems in China and other Asian countries (WHO 2003; Popkin 2006; Popkin, Kim et al. 2006; Liu 2007). Although body mass index (BMI)[1] cutoffs of 25 and 30 kg/m$^2$ for overweight and obesity, respectively, have been widely used among Western populations and recommended by the World Health Organization as international criteria for body fatness at the population level (WHO expert committee 1995), controversy remains about the optimal BMI cutoffs for Asians (Misra 2003; Stevens 2003; WHO expert consultation 2004).

Most of the work that serves as background for these debates used (a) cross-sectional samples and (b) a *P*-value $< 0.05$ or non-overlapping 95% confidence intervals (95% CI) as a decision rule (Misra 2003; Stevens 2003; WHO expert consultation 2004). Because *P*-values and 95% CI widths are driven by both magnitude of effect and sample size (Weinberg 2001), findings will vary by sample size, BMI distributions, and prevalence of risk factors. A BMI cutoff of 23 kg/m$^2$ has been proposed by some authors, who used sensitivity, specificity, and receiver operating characteristic (ROC) curve analysis (Bei-Fan 2002; Ho, Lam et al. 2003; Wildman, Gu et al. 2004; Weng, Liu et al. 2006; Huxley, James et al. 2008). Because these studies were based on cross-sectional samples, we are not certain that the exposure to a

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[1] Abbreviation used: AUC, area under the curves; BMI, body mass index; CHNS, China Health and Nutrition Survey; ROC, receiver operating characteristic.

higher BMI had preceded the hypertension outcome (Grimes and Schulz 2002). We used an ROC curve analysis to determine an optimal BMI cutoff for overweight that represents elevated incidence of hypertension in Chinese adults.

## 5.3. Subjects and Methods

### *5.3.1. Subjects*

The China Health and Nutrition Survey (CHNS) is an ongoing study established in the late 1980s in nine provinces that vary substantially in geography, economic development, public resources, and health indicators. A detailed description of the study design and data collection procedures has been presented elsewhere (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). Data sets and questionnaires may be downloaded from the CHNS websites (http://www.cpc.unc.edu/china). For this analysis, we used data from the CHNS conducted in 2000 and 2004 because these two surveys had the most comparable study sample, questionnaires, and protocol and equipment in measuring blood pressure, weight, height, and waist circumference. Of 6162 participants who were 18–65-year-old men, non-pregnant or non-lactating women in 2000 and who were involved in both surveys, 5543 (90%) had complete and plausible measurements of blood pressure and other anthropometric measurements (e.g., 4-year changes in height < 10 cm and in BMI < 10 kg/m$^2$; a baseline BMI of 15–40 kg/m$^2$, waist circumference of 45–150 cm, waist-to-hip ratio of 0.6–1.3, and hip circumference of 55–155 cm; or the difference between systolic and diastolic blood pressure < 10 mmHg). Of the 5543 participants, 4492 (81%) with normal blood pressure in 2000 were included in our longitudinal sample. We only included 18–65-year-old adults, non-pregnant, and non-lactating women because a teenager, an older person, or a pregnant or lactating woman requires different BMI cutoffs (WHO expert committee 1995). The exclusion of participants with extreme or implausible values of anthropometric measures or blood pressure helped to increase estimate precision without changing overall results.

### *5.3.2. Measurements*

Three blood pressure measures were taken in seated position and on the right arm by trained health workers who followed a standardized procedure using regularly calibrated mercury sphygmomanometers with appropriate-sized cuffs. Systolic blood pressure was measured at the first appearance of a pulse sound (Korotkoff phase 1) and diastolic blood pressure at the disappearance of the pulse sound (Korotkoff phase 5). Three measurements of systolic or diastolic blood pressure were averaged to reduce the effect of measurement errors. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed by a doctor (Chobanian, Bakris et al. 2003). We did not include the use of an antihypertensive medication to define hypertension because in this sample, only a small proportion of Chinese adults was diagnosed (< 5%) or treated (< 3%) with any antihypertensive medications; and none used the medications without being diagnosed by a doctor. Moreover, sensitivity analysis showed that incorporating these measures produced similar findings but with a smaller sample size. Cumulative incidence was calculated by dividing new cases of hypertension over the study period by the total at-risk population, aged 18–65 years, in 2000.

BMI ($kg/m^2$) was calculated based on weight and height, which were measured by trained health workers who followed standardized procedures and used regularly calibrated equipment (SECA 880 scales and SECA 206 wall-mounted metal tapes) (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). Waist circumference was measured using a non-elastic tape at a point midway between the lowest rib margin and the iliac crest in a horizontal plane. Hip circumference was measured at the point yielding the maximum circumference over the buttocks. Covariates such as age, sex, smoking habits, alcohol consumption, and place of residence were collected by direct interviews.

### *5.3.3. Statistical analysis*

We used Poisson regression models to examine the association between BMI and hypertension. Potential confounding factors at baseline, such as age (centered at 40 years), sex, smoking habits (dichotomized to never-smoker or ever-smoker), alcohol consumption (dichotomized to current drinker or non-drinker), place of residence (urban or rural), and waist circumference were taken into account in regression models. A covariate was considered as an effect-measure modifier if its interaction term with BMI in regression models had a *P*-value $< 0.15$ (chi squared test) or as a confounder if it caused a change in incidence ratios of more than 10%. Based on these criteria, the most reduced model had age as an effect-measure modifier (the association between BMI and hypertension was stronger among the younger participants); and sex and drinking status as confounding factors. We purposely stratified our analyses by sex to make them comparable with other studies.

To evaluate an optimal BMI cutoff, we computed and looked for the shortest distance on the sex-specific receiver operating characteristic (ROC) curve, estimated at each half unit of BMI. A distance on the ROC curve is equal to $\sqrt{(1-sensitivity)^2 + (1-specificity)^2}$ (Weng, Liu et al. 2006). Crude and adjusted area under the ROC curves (AUC) were estimated by using logistic regression models. Given the large sample size of the cohort, also we performed stratified analyses by age group. We used two-tail independent t-tests to compare two means and chi squared tests to compare different levels or trends of categorized variables. The attributable population risk was estimated by summing exposure-specific attributable fractions. We conducted all analyses using Stata software version 9.2 (Stata Inc., TX, USA).

### *5.3.4. Role of the funding sources and ethical consideration*

The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The sponsors were not involved in the study design, the collection, analysis, or interpretation of data, the writing or submission of the manuscript for publication. Written informed consent was obtained from each participant for each CHNS round. The Institutional Review Boards (IRB) of the School of Public Health, University of North Carolina at Chapel Hill and the Chinese Center for Disease Control and Prevention reviewed and approved the study.

## 5.4. Results

At baseline, mean systolic and diastolic blood pressures were higher among men compared to women (about 3 mmHg; $P < 0.05$). Women had a higher mean BMI and prevalence of overweight compared to men. The proportions of Chinese men who were smokers (63%) and alcohol drinkers (65%) were much higher than those of women (4 and 10%, respectively) (**Table 5.1**).

Although the Chinese adults had a low mean BMI (a mean of 22.6 kg/m$^2$; 95% CI: 22.5–22.7), four-year cumulative incidences of hypertension in women and men were 12.7% (95% CI: 11.3–14.0) and 18.7% (95% CI: 17.1–20.4), respectively. In general, about one fourth of the hypertensive new cases in the Chinese population are attributed to a BMI of 23 kg/m$^2$ or higher. In addition, a higher population attributable risk was found in women and young participants. Crude incidence of hypertension among men was statistically higher than that of women at almost all BMI levels (e.g., 21–22.9, 23–24.9, and 25–29.9; $P < 0.05$). There is a decline in hypertension incidence at the BMI of 30–40 kg/m$^2$ in men. The estimate, however, might not reflect a real trend of BMI and hypertension association because of a small number of participants that lead to less precise estimate in the BMI group (**Fig. 5.1***A*). The adjusted incidence of hypertension in men (in a hypothesized population at age of 40 years) was statistically higher than that of women at all BMI levels (Fig. 5.1*B*).

The AUC for the prediction of hypertension by BMI (about 0.62) was significantly higher than what would be expected by chance, which indicated that BMI predicts hypertension. The AUC values were higher in younger compared to older participants (**Table 5.2**). Compared to the maximum value of AUC (1.0 for perfect prediction), these AUC values suggested that other risk factors also contributed to the prediction of hypertension. Controlling for age and other potential confounding factors, the AUC increased significantly to about 0.70, without reducing estimated precision.

In this cohort, BMI levels of 23.5 kg/m$^2$ for women and of 22.5 kg/m$^2$ for men provided the shortest distance on the ROC curves (corresponding to a sensitivity and specificity of about 60%). The optimal BMI cutoff for ages 41–65 years was slightly higher compared to that for age 18–40 years. A BMI cutoff of 25 provided lower sensitivities (26–37%) and higher specificities (76–86%) compared to the optimal BMI cutoffs (Table 5.2). **Fig. 5.2***A*, *B, C* illustrate ROC curves and optimal BMI levels in different age and sex groups.

### 5.5. Discussion

To our knowledge, we are the first to use ROC curve analyses to identify an optimal BMI cutoff for incident hypertension in an Asian sample. Our findings show a strong positive association between BMI and incidence of hypertension and suggest an optimal BMI cutoff of about 23.0 kg/m$^2$ to define overweight in 18–65-year-old Chinese adults.

The significant trend of increased risk of hypertension with increased BMI is similar to results from cross-sectional studies in Asian populations (Ho, Chen et al. 2001; Colin Bell, Adair et al. 2002; Lin, Lee et al. 2002; Wildman, Gu et al. 2004; Weng, Liu et al. 2006; Tesfaye, Nawi et al. 2007). This longitudinal analysis of hypertension incidence confirms a dose-response relationship. Using the CHNS 2000–2004 cohort, Li et al. (Li, Zhai et al. 2007) also found higher hypertension incidence with higher BMI and waist circumference levels. Although both studies were based on data from the same cohort, they differ in focus. Our focus was on establishing optimal BMI cutoffs; while theirs was on comparing hypertension incidence or risk ratios among several BMI and waist circumference groups (Li, Zhai et al. 2007).

Our study suggests an optimal BMI cutoff of less than 25 kg/m$^2$ for 18–65-year-old Chinese men and women. We found a slightly increase in the BMI cutoffs (about 0.5 kg/m$^2$) among older compared to younger participants. There are several explanations for the lower optimal BMI cutoff for Asians compared to that of Westerners. First, Asian ethnicities tend to have a higher total body fat (Wang, Thornton et al. 1994; Deurenberg, Deurenberg-Yap et al. 2002) as well as a greater amount of abdominal and visceral fat (Park, Allison et al. 2001; Lear, Humphries et al. 2007) at a given BMI compared to other races and ethnicities. Increased visceral fat mass leads to increased blood pressure via several mechanisms such as leptin resistance, insulin resistance, and inflammation (Kaplan 2006; Sniderman, Bhopal et al. 2007). Second, race/ethnic groups often differ in socioeconomic status, cultural factors, food habits, physical activity levels, and lifestyles (Bell, Adair et al. 2004; Merlo, Asplund et al. 2004). Third, different ethnicities may have different combinations of genes associated with hypertension and gene-environment interactions that lead to the variation in blood pressure (Carretero and Oparil 2000; Luft 2001; Maca-Meyer, Gonzalez et al. 2001; Cui, Hopper et al. 2002; Kaplan 2006). Finally, there is also speculation that insults during fetal development and infancy might have also resulted in the elevated risks. However, there is great debate about these relationships and their subsequent effects (Barker 2002; Williams and Poulton 2002; Adair and Cole 2003; Demerath, Cameron et al. 2004; Singhal and Lucas 2004).

Our findings were consistent with results from large-scale cross-sectional studies in Chinese and Indian populations (Bei-Fan 2002; Lin, Lee et al. 2002; Wildman, Gu et al. 2004; Mohan, Deepa et al. 2007). In those studies, a BMI cutoff of 22–24 kg/m$^2$ was associated with an increase in prevalence of hypertension, diabetes mellitus, dyslipidemia, and cardiovascular diseases. Huxley et al. (Huxley, James et al. 2008), in a sample of 263000 participants (73% Asian) from 21 cross-sectional studies in Australia and some Asian countries, also show an optimal BMI cutoff of about 24 kg/m$^2$ for Asians.

Our proposed optimal BMI cutoff was lower than those suggested by authors who used total mortality as a study outcome in some Chinese longitudinal samples (Zhou 2002; Gu, He et al. 2006). In those samples, a BMI of 24–24.9 kg/m$^2$ in men, 25–26.9 kg/m$^2$ in women (Gu, He et al. 2006), and 24–27.9 kg/m$^2$ in both sexes (Zhou 2002) was associated with the lowest mortality rate. There are several potential explanations for the differences.

First, at baseline, participants were much older in the studies by Gu et al. (Gu, He et al. 2006) (≥ 40 year-olds; a mean age of 56 years) and by Zhou (Zhou 2002) (≥ 30 year-olds, a mean age of 47 years) compared to ours (18–65 year-olds, a mean age of 42 years). The inclusion of an older participant would lead to (a) an increase in BMI due to the naturally decreased height and (b) a larger influence of other cardiovascular risks. Thus, the inclusion of an older participant would bias the association between BMI and health outcome toward the null and lead to a higher BMI cutoff. Second, mortality is influenced by factors other than BMI (e.g., diseases and pre-existing health conditions, HIV/AIDS, smoking habits, alcohol consumptions, other lifestyles factors, accidents, suicides, and health care services) (Misra 2003; Stevens 2003). Thus, we would see a higher BMI cutoff for an all-cause mortality outcome compared to hypertension or other cardiovascular risk. Third, in the studies by Gu et al. (Gu, He et al. 2006) and Zhou (Zhou 2002), the differences in death rates or risk ratios between different BMI levels were negligible (most of them had an overlapping 95% CI or a $P$-value > 0.05).

Even though the use of longitudinal data was a strength of our study, participant selection for this analysis sample may reduce the generalizability of the findings. This sample included only: (a) participants of both surveys (2000 and 2004), who tended to be older; and (b) normotensive participants in 2000, who tended to have a lower risk of hypertension (and associated risk factors, e.g., being a younger or female; having a lower BMI or smaller waist circumference; or less likely to smoke or drink alcohol). The inclusion of older participants, who had additional risk factors other than increased BMI, would bias the estimate for the association between BMI and hypertension toward the null and decrease the AUC values. In contrast, the inclusion of persons with a lower risk of hypertension in the longitudinal sample would bias the estimate away from the null and increase the AUC values.

Since a sensitivity analysis showed that optimal BMI cutoffs by level of risk factors such as age, smoking, or drinking status were similar to the overall sex-specific BMI cutoffs, selection bias was not likely to be a notable problem in this sample. Even though this participant selection did not affect our overall results, it would be better to have an open cohort to measure an incidence density, based on the number of new cases and total person-time at risk. However, we were not able to estimate the incidence density of hypertension in the CHNS samples because the exact time when the hypertension outcome occurred was unknown.

Similar to other cardiovascular risk factors, blood pressure might vary over time (Chobanian, Bakris et al. 2003), and thus, a hypertensive patient in one survey could become normotensive in the next survey. In our study, the exclusion of hypertensive patients in 2000 would lead to a decrease in the mean blood pressures in 2000, and thus, lead to an increase in hypertension incidence. The findings need verifications from further studies that use other outcomes such as incidence of diabetes mellitus, dyslipidemia, cardiovascular disease events or mortality. Although BMI is positively associated with increased risk of cardiovascular risk, its predictions for those outcomes are moderate (AUC of 0.6–0.8) in Asian populations (Lin, Lee et al. 2002; Ho, Lam et al. 2003; Weng, Liu et al. 2006; Huxley, James et al. 2008). The moderate levels of AUC indicate that other factors also contribute to the prediction of cardiovascular risk. Thus, the BMI cutoff based on the sensitivity-specificity approach (a) is considered as a useful threshold to define overweight for public health and clinical recommendations and actions and (b) is not considered as the screening level for cardiovascular disease risk.

It is uncertain if the optimal BMI cutoffs, based on the longitudinal sample of Chinese adults, could be extrapolated to other Asian countries because Asians differ from each other in the association between BMI and non-communicable diseases. As noted earlier, Asian subpopulations may have different combinations of genes associated with hypertension and different gene-environment interactions that lead to a variation in blood pressure (Carretero and Oparil 2000; Luft 2001; Maca-Meyer, Gonzalez et al. 2001; Cui, Hopper et al. 2002; Macaulay, Hill et al. 2005; Kaplan 2006). There is a tendency of genotype clustering among residents in (a) the South Asia and some Southeast Asia (e.g., Thailand, Malaysia, and apart of Indonesia); (b) East Asia (e.g., China, Japan, and Korea) and some Southeast Asia (Vietnam, the Philippines, and apart of Indonesia) (Maca-Meyer, Gonzalez et al. 2001; Macaulay, Hill et al. 2005). In combination with differences in environment, we might expect different associations between BMI and health risks in those countries.

In conclusion, this study suggests BMI values of 23.5 $kg/m^2$ in women and 22.5 $kg/m^2$ in men may be more appropriate for defining overweight in Chinese adults. Consistent with other cross-sectional studies, this study suggests that earlier prevention of excessive weight gain is needed to reduce hypertension in this population. Early prevention and control of hypertension and overweight are considered a cost-effective approach to decrease economic and health burdens of non-communicable diseases worldwide (WHO 2003).

**Table 5.1.** Characteristics of 18–65-year-old, normotensive participants in 2000[1]

| | Women (n = 2415) | | Men (n = 2077) | |
|---|---|---|---|---|
| | Estimate | 95% CI | Estimate | 95% CI |
| Age, *y* | 42.5 | (42.1–42.9) | 41.5* | (41.0–41.9) |
| Systolic blood pressure, *mm Hg* | 111.7 | (111.2–112.1) | 115.2* | (114.7–115.7) |
| Diastolic blood pressure, *mm Hg* | 73.0 | (72.7–73.4) | 75.5* | (75.2–75.9) |
| Body mass index, *kg/m²* | 22.8 | (22.6–22.9) | 22.4* | (22.3–22.5) |
| 15–18.5 kg/m², *%* | 6.0 | (5.1–7.0) | 6.0 | (5.0–7.0) |
| 23–40 kg/m², *%* | 44.0 | (42.0–46.0) | 38.1* | (36.0–40.2) |
| 25–40 kg/m², *%* | 21.7 | (20.0–23.3) | 17.5* | (15.9–19.2) |
| Ever-smoke cigarettes, *%* | 3.6 | (2.9–4.4) | 62.9* | (60.8–65.0) |
| Alcohol drinker, *%* | 10.2 | (8.9–11.4) | 64.7* | (62.6–66.8) |
| Urban resident, *%* | 32.4 | (30.6–34.3) | 32.2 | (30.2–34.2) |

[1] Values are means or percentages with 95% CI, n = 4492 (excluded participants with implausible anthropometric indices e.g., BMI < 15 or > 40 $kg/m^2$)

[*] $P < 0.05$, compared to women; two-tail independent t-test for continuous variables or chi squared test for categorized variables.

**Table 5.2.** Area under the receiver operating characteristic curves (AUC), optimal body mass index (BMI) cutoff values, sensitivities, and specificities stratified by sex and age at baseline for the prediction of hypertension incidence

| | | | Optimal BMI cutoffs (kg/m$^2$) | | | At a BMI of 25 (kg/m$^2$) | |
|---|---|---|---|---|---|---|---|
| | n | AUC[1] | Cutoffs | Sensitivity | Specificity | Sensitivity | Specificity |
| **Both sexes** | | | | | | | |
| All ages | 4492 | 0.61 | 22.5 | 0.62 | 0.56 | 0.32 | 0.82 |
| 18–40 y | 1999 | 0.64 | 22.5 | 0.63 | 0.61 | 0.33 | 0.85 |
| 41–65 y | 2493 | 0.59 | 23 | 0.56 | 0.57 | 0.31 | 0.80 |
| **Women** | | | | | | | |
| All ages | 2415 | 0.62 | 23.5 | 0.56 | 0.65 | 0.36 | 0.80 |
| 18–40 y | 1053 | 0.64 | 23 | 0.59 | 0.66 | 0.31 | 0.85 |
| 41–65 y | 1362 | 0.59 | 23.5 | 0.57 | 0.58 | 0.37 | 0.76 |
| **Men** | | | | | | | |
| All ages | 2077 | 0.62 | 22.5 | 0.61 | 0.59 | 0.29 | 0.85 |
| 18–40 y | 946 | 0.64 | 22.5 | 0.62 | 0.62 | 0.34 | 0.86 |
| 41–65 y | 1131 | 0.61 | 22.5 | 0.60 | 0.57 | 0.26 | 0.84 |

[1] AUC values range from 0.5 (no prediction) to 1.0 (perfect prediction)

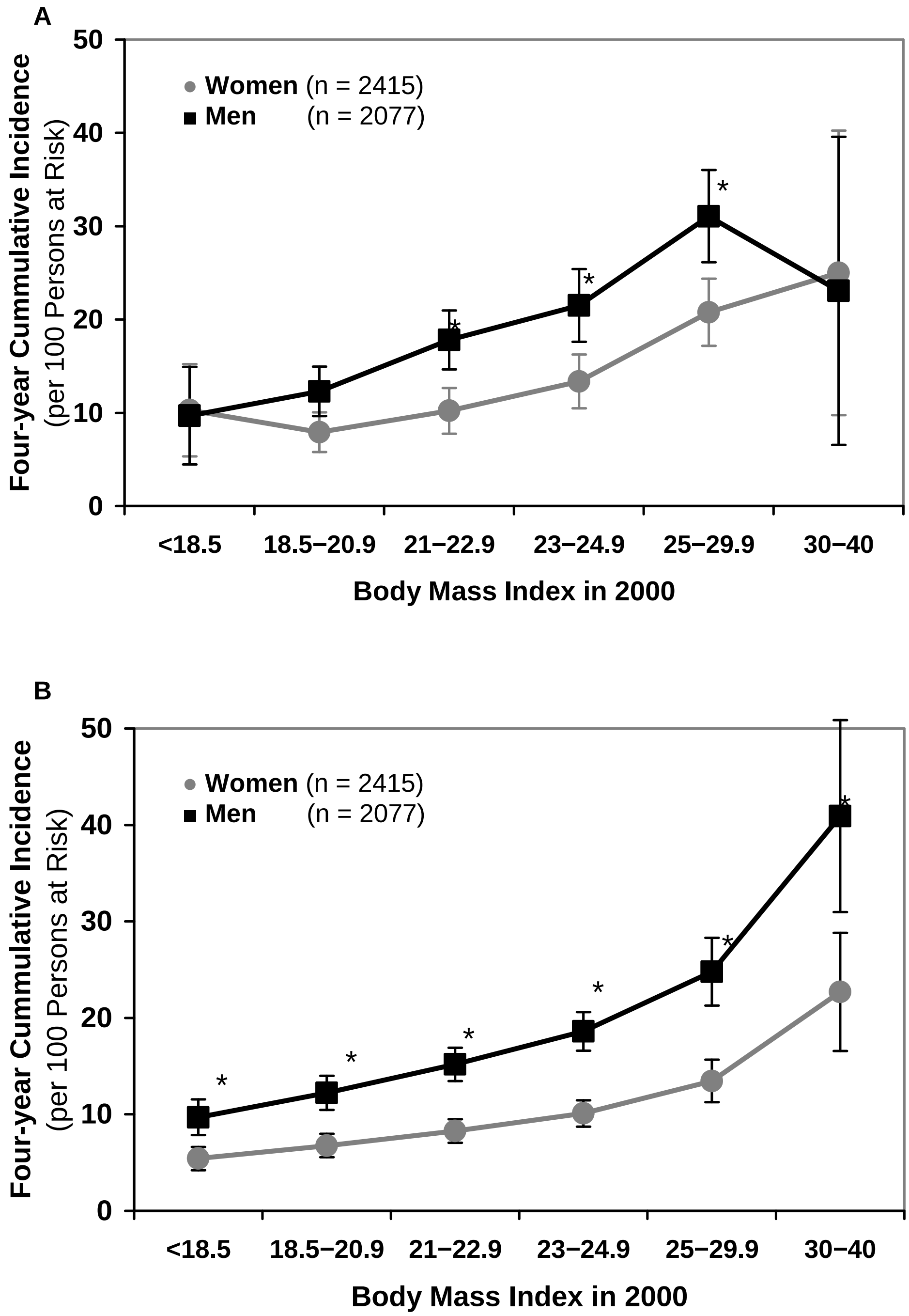


**Figure 5.1.** Four-year cumulative incidence and 95% CI of hypertension (new cases / 100 persons at risk) by body mass index levels in 2000. A, crude incidence; B, adjusted incidence in a hypothesized population at age of 40 years
* *P* < 0.05 chi squared test, compared to women; *P*-trend < 0.005 for all

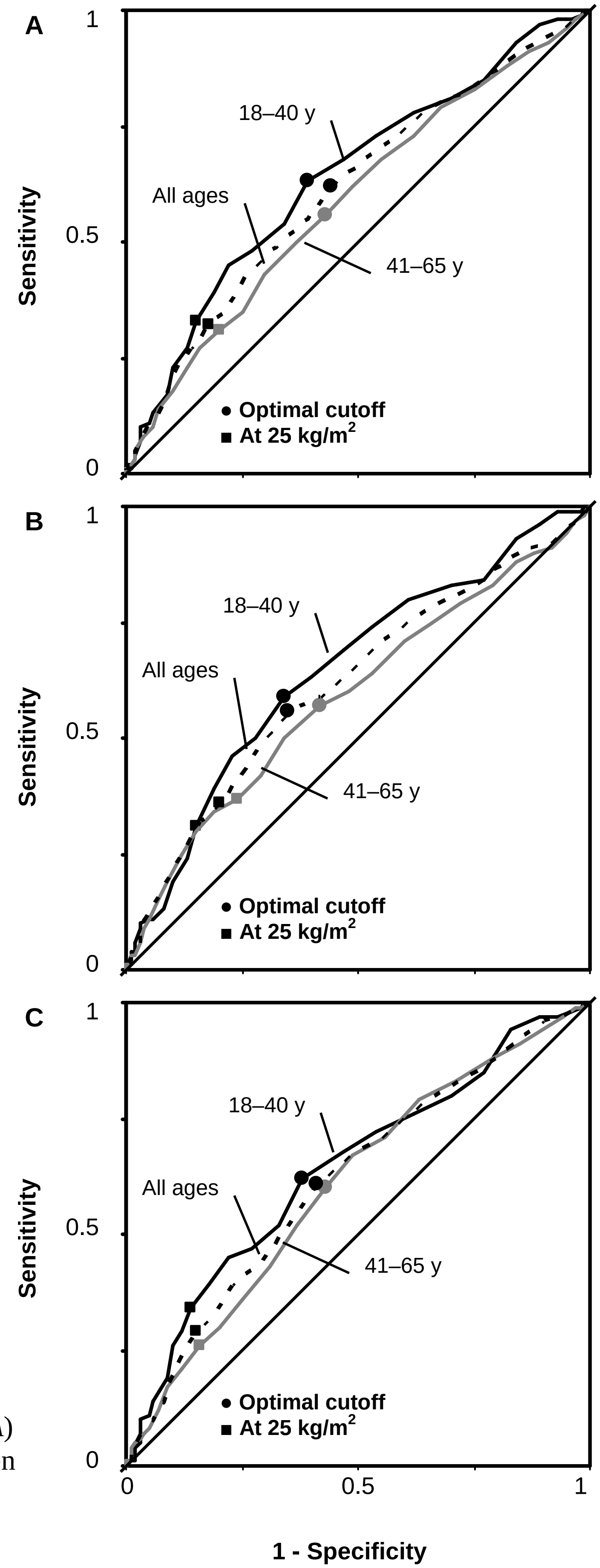


**Figure 5.2.** ROC curves for the prediction of hypertension by BMI and age groups. (*A*) in both sexes; (*B*) in women; and (*C*) in men

# CHAPTER 6. PREDICTION OF HYPERTENSION BY DIFFERENT ANTHROPOMETRIC INDICES IN ADULTS

## 6.1. Abstract

*Objectives:* To (a) compare the prediction of hypertension by waist circumference (WC), waist-to-stature ratio (WSR), or waist-to-hip ratio (WHR) to that by BMI and (b) determine if WC, WSR, or WHR adds to the prediction of hypertension by BMI among Chinese adults.

*Methods and Procedures:* We included 7,336 Chinese adults aged 18–65 years who participated in the 2004 China Health and Nutrition Survey. A change of ≥ 10% in the prevalence ratio of BMI (PR) or area under the curve (AUC) when WC, WSR, or WHR was added to a model with BMI was used as the criterion for significant contribution to the prediction of hypertension by BMI. If AUC of WC, WSR, or WHR was ≥ 10% larger than that of BMI, it was considered as a better predictor.

*Results:* The prevalence of hypertension (17 and 23% for women and men, respectively) was significantly related to increased BMI, WC, WSR, and WHR ($P$ for trend < 0.001). Although there was a better model fit when WC, WSR, or WHR was added to a model with BMI ($P$ < 0.05; likelihood ratio test), the changes in PR and AUC were < 10% and < 5%, respectively. The sex-specific AUC for the prediction of hypertension by BMI (of 0.7–0.8) was similar to that by WC, WSR, or WHR.

*Conclusions:* WC, WSR, and WHR did not perform better than BMI or add to the prediction of hypertension by BMI. BMI appears to be sufficient to screen for increased prevalence of hypertension among 18–65-year-old Chinese adults.

## 6.2. Introduction

Anthropometric indicators for body fat are widely used to predict chronic disease risk in individual and population levels. Compared to body mass index (BMI)—a good indicator for body fatness in adults at the population level, waist circumference (WC), waist-to-stature ratio (WSR), and waist-to-hip ratio (WHR) provide additional information about central fat distribution (Gibson 2005; Klein, Allison et al. 2007). Studies aimed to determine whether WC, WHR, and WSR predict hypertension better than BMI or add to the prediction of hypertension have shown controversial results in both Western (Visscher, Seidell et al. 2001; Zhu, Wang et al. 2002; Benetou, Bamia et al. 2004) and Asian populations (Ho, Chen et al. 2001; Lin, Lee et al. 2002; Ho, Lam et al. 2003; Hsieh, Yoshinaga et al. 2003; Ito, Nakasuga et al. 2003; Wildman, Gu et al. 2005; Sakurai, Miura et al. 2006). As criteria for judging predictions of alternate indicators, these studies used a larger point estimate, a $P$-value < 0.05, or a non-overlap of 95% confidence intervals (95% CI). Because $P$-values and 95% CI are driven by both magnitude of effect and sample size (Weinberg 2001), different conclusions would result from different sample sizes or BMI distributions.

This study is a comparison of the predictive ability of these alternate indicators as they relate to Chinese adults. We utilized two criteria that are less affected by sample size: the difference in prevalence ratio and area under the curve (AUC) to (a) compare the prediction of hypertension by WC, WSR, or WHR to that by BMI and (b) determine if WC, WSR, or WHR added to the prediction of hypertension by BMI among 18–65-year-old Chinese adults.

## 6.3. Methods and Procedures

### *6.3.1. Participants*

We used data from the China Health and Nutrition Survey (CHNS) conducted in 2004 with a representative sample drawn from the nine provinces in China (Guangxi, Guizhou, Heilongjiang, Henan, Hubei, Hunan, Jiangsu, Liaoning, and Shandong). This sample was diverse with variation found in a wide-ranging set of socioeconomic factors (income, employment, education and modernization) and other related health, nutritional and demographic measures (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). Of the 8,258 participants aged 18–65 years who were men, non-pregnant or non-lactating women, 7,336 (89%) had complete and plausible measurements of weight, height, blood pressure, WC, and hip circumference (HC) (e.g., BMI of 15–35 kg/m$^2$, weight of 30–150 kg, height of 130–190 cm, WC of 45–150 cm, HC of 55–155 cm, WHR of 0.6–1.1, and the difference between systolic and diastolic blood pressure < 10 mmHg). We only included 18–65-year-old adults, non-pregnant, and non-lactating women because adolescents, the elderly, and pregnant or lactating women require different BMI and WC cutoffs (WHO expert committee 1995). The exclusion of participants with extreme values in anthropometric measurements and blood pressure helped to increase the estimate precision without changing the overall results.

### *6.3.2. Study design*

Three blood pressure measurements were taken in a seated position and on the right arm by trained health workers who followed a standardized procedure using regularly calibrated mercury sphygmomanometers with appropriate-sized cuffs. Systolic blood pressure was measured at the first appearance of a pulse sound (Korotkoff phase 1) and diastolic blood pressure at the disappearance of the pulse sound (Korotkoff phase 5). Three measurements of systolic or diastolic blood pressure were averaged to reduce the effect of measurement error. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥ 90 mmHg, or being previously diagnosed by a doctor (Chobanian, Bakris et al. 2003). The definition of hypertension was not based on the use of an antihypertensive medication because in this sample, a small proportion of Chinese adults was diagnosed (< 7%) or treated (< 5%) with an antihypertensive medication and none used an antihypertensive medication without being diagnosed by a doctor. Moreover, sensitivity analysis showed that incorporating these measures produced similar findings.

BMI was calculated based on weight and height measured by trained health workers who followed standardized procedures using regularly calibrated equipment (SECA 880 scales and SECA 206 wall-mounted metal tapes). The health workers used non-elastic tape to measure WC at a point midway between the lowest rib and the iliac crest in a horizontal plane and HC at the point yielding the maximum circumference over the buttocks (Popkin, Paeratakul et al. 1995; CPC-UNC 2007). Waist-to-stature ratio (WSR = WC / height) and waist-to-hip ratio (WHR = WC / HC) were calculated based on the measured WC, height, and HC. Covariates, such as age, sex, smoking habits, alcohol consumption, and place of residence were collected by direct interviews.

### *6.3.3. Statistical analysis*

We used Poisson regression models to examine the association between BMI and hypertension. Potential confounding factors, such as age (centered at the mean age of 45 years), sex, smoking habits (dichotomized to never-smoker or ever-smoker), alcohol consumption (dichotomized to current drinker or non-drinker), and place of residence (urban or rural) were also taken into account in regression models. A covariate was considered as an effect measure modifier if its interaction term with BMI in regression models had a *P*-value < 0.15 (chi squared test) or as a confounder if it caused a change in prevalence ratios of BMI (PR) of ≥ 10%. Based on those criteria, age was the only effect measure modifier and there were no confounders. To make our results comparable with those of other studies, we stratified our analyses by sex in crude, age-adjusted, and age-specific models. BMI, WC, WSR, and WHR were kept in continuous scale to maximize the power of statistical tests.

To determine if the inclusion of WC, WSR, or WHR improved the prediction of hypertension by BMI, we estimated the change in sex-specific PR (from Poisson regression models) and sex-specific AUC (from logistic regression models) between a model with BMI + WC, BMI + WSR, or BMI + WHR to a model with BMI alone. A change in PR or AUC of ≥ 10% was used as a criterion for a significant contribution of WC, WSR, or WHR to the prediction of hypertension by BMI. We separately compared sex-specific AUC between a model with WC, WSR, or WHR to a model with BMI to examine if any was better than BMI in predicting hypertension; an increase of ≥ 10% in AUC was used as a criterion for a superior prediction. We used the criterion of ≥ 10% because it is arbitrarily used to determine a notable confounding factor.

The fit of a model with BMI was compared to that of a model with BMI + WC, BMI + WSR, or BMI + WHR. A *P*-value < 0.05 (likelihood ratio test) was used as the criterion for a significant increase in model fit. To evaluate if these findings were consistent at different BMI levels, we performed similar analyses for participants with a BMI < 23 kg/m$^2$ and BMI ≥ 23 kg/m$^2$ (data were presented in Supplementary Table 1 and 2). All analyses were performed using Stata software version 9.2 (Stata Inc., TX, USA).

#### *6.3.4. Role of the funding sources and ethical consideration*

The authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The sponsors were not involved in the study design, the collection, analysis or interpretation of data, writing of the manuscript, or decision to submit the manuscript for publication. Written informed consent was obtained from each participant for each CHNS round. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The Institutional Review Boards (IRB) of both the School of Public Health, University of North Carolina at Chapel Hill and the Chinese Center for Disease Control and Prevention have reviewed and approved the study.

### 6.4. Results

Crude prevalence of hypertension among men of 23.0% (95% CI: 21.6–24.4) was higher than among women (16.8%; 95% CI: 15.6–18.0; *P* < 0.001). Means systolic and diastolic blood pressures were higher among men (122 and 80 mmHg, respectively) compared to women (118 and 77 mmHg; *P* < 0.001). Only a small proportion of the Chinese adults was diagnosed or treated with any antihypertensive medication (about 5%). A small proportion of hypertensive participants, identified by measured blood pressures, was diagnosed by a doctor (35%) or treated with an antihypertensive medication (25%). Men and women had similar means (23 kg/m$^2$) and distribution of BMI. Men had higher means WC, HC, and WHR, but a smaller mean WSR compared to women. The proportions of Chinese men who were smokers (58.8%) and alcohol drinkers (62.3%) were much higher than those of women (**Table 6.1**).

There was a significant trend of increased prevalence of hypertension with an increase in BMI, WC, WSR, or WHR (*P* for trend < 0.001) for both men and women (**Fig. 6.1**).

On average, each unit increase in BMI was associated with an 18% and 14% increase in PR for hypertension in women and men, respectively (*P* < 0.001; crude models). There was about 15% increase in PR associated with each unit increase in BMI in age-adjusted or age-specific models (*P* < 0.001). Although there was an increase in model fit when adding WC, WSR, or WHR to a model with BMI (*P* < 0.05 in almost all of the models; likelihood ratio test), the changes in PR were < 10% in the crude models and < 5% in the age-adjusted and age-specific models (**Table 6.2**). The changes in PR increased slightly (< 10% except for WSR in the crude model for women) among participants with a BMI < 23 kg/m$^2$ (**Supplementary Table 6.1**).

The AUC estimates for the prediction of hypertension by BMI were about 0.7–0.8 and were higher among women (*P* < 0.05 in age-adjusted and age-specific estimates). Although there was an increase in model fit when adding WC, WSR, or WHR to a model with BMI (*P* < 0.05 in almost all of the models; likelihood ratio test), the changes in AUC were < 5% in the crude models and < 1% in the age-adjusted and age-specific models (**Table 6.3**). The changes in AUC increased slightly (< 10% except for WSR in crude model for women) among participants with a BMI < 23 kg/$m^2$ (**Supplementary Table 6.2**).

Models with WC or WSR provided similar AUC compared to models with BMI for men, women, and both sexes (% difference in AUC < 2.5%; $P > 0.05$). A model with WHR had about 4–10% lower in AUC compared to a corresponding model with BMI (**Table 6.3**). There were some increases (< 10% except for WSR in crude model for women) in the prediction of hypertension by WC, WSR, and WHR compared to that BMI among participants with a BMI < 23 kg/$m^2$ (**Supplementary Table 6.2**).

## 6.5. Discussion

To our knowledge, we are the first to use the changes in PR and AUC as criteria to evaluate if WC, WSR, or WHR adds to the prediction of hypertension by BMI in an Asian population. Our findings show that even though WC, WSR, and WHR are predictors of hypertension and improve the fit of models with BMI, they do not perform better than BMI or add meaningfully to the prediction of hypertension outcome by BMI.

We observed a significant trend of increased prevalence of hypertension with increased BMI, WC, WSR, and WHR. This finding was similar to results from studies in Asian (Ho, Chen et al. 2001; Colin Bell, Adair et al. 2002; Lin, Lee et al. 2002; Ho, Lam et al. 2003; Ito, Nakasuga et al. 2003; Wildman, Gu et al. 2004; Weng, Liu et al. 2006; Balkau, Deanfield et al. 2007; Tesfaye, Nawi et al. 2007) and Western populations (Zhu, Wang et al. 2002; Dalton, Cameron et al. 2003; Canoy, Luben et al. 2004). Increased blood pressure is associated with increased BMI because an increase in body weight and thus BMI related to an increase in body fluid volume, in peripheral resistance (e.g., hyperinsulinemia, cell membrane alteration, and hyperactivity of the rennin-angiotensin system lead to functional constriction and structural hypertrophy), and in cardiac output (Kaplan 2006). The positive correlation between WC, WSR, or WHR and prevalence of hypertension could be explained by an increase in visceral fat that lead to increased leptin and insulin resistance and worse lipid profiles (Kaplan 2006; Pavey, Plalmer et al. 2006).

There are several possible explanations for the finding that WC and WSR did not add to the prediction of hypertension by BMI. First, WC and WSR were highly correlated with BMI (sex-specific Pearson correlation coefficients were about 0.75). The high correlation leads to a large overlap among the predictions explained by WC, WSR, and BMI. Second, compared to other races and ethnicities, Asians would accumulate more total body fat and visceral fat with an increase in body weight (Park, Allison et al. 2001; Deurenberg, Deurenberg-Yap et al. 2002; Lear, Humphries et al. 2007). In addition, WC and WSR are only proxy indicators for total body fat and visceral fat (Gibson 2005) while increased visceral fat is a predictor for an increase in metabolic risk (Klein, Allison et al. 2007).

Our study showed a tendency toward increased prediction of hypertension by WC, WSR, or WHR among participants with a lower BMI (e.g., BMI $< 23$ kg/m$^2$). The finding is consistent with those from Ardern et al. (Ardern, Janssen et al. 2004) in which the association between WC and the cardiovascular risk was stronger at a lower BMI. However, the studies are not directly comparable. Their sample included American (White, Black, and Hispanic) and Canadian participants who differed from our Chinese participants in age, body composition, lifestyles, and socio-economic characteristics. Also, Ardern et al. (Ardern, Janssen et al. 2004) used the Framingham coronary heart disease risk index as study outcome, while we used hypertension.

We would have concluded that WC, WSR, or WHR added to the prediction of hypertension by BMI (this finding was consistent with other studies (Zhu, Wang et al. 2002; Ito, Nakasuga et al. 2003; Wildman, Gu et al. 2005)) if a *P*-value < 0.05 of a likelihood ratio test was used as a decision criterion. However, the criterion is not the best choice because a *P*-value varies with both sample size and magnitude of effect (Weinberg 2001).

The findings that WC, WSR, and WHR were not superior to BMI in the prediction of hypertension were consistent with those from a representative sample of 55,563 Taiwanese in a study by Lin et al. (Lin, Lee et al. 2002). Their protocols for the measurements of weight, height, WC, HC, and blood pressures were similar to ours. Based on their data, we computed the difference in AUC based on the sex-specific AUC of each risk factor or disease condition (e.g., hypertension, diabetes mellitus, dislipidemia, elevated triglyceride, total cholesterol, low density lipoprotein, or decreased high density lipoprotein). WC, WSR, or WSR was not superior (< 10% increase in AUC) to BMI in the prediction of any risk factors or disease conditions in women or men.

We also computed the difference in AUC with the use of sex-specific AUC from a sample of 2,895 Hong Kong Chinese in a study by Ho et al. (Ho, Lam et al. 2003). WC provided similar predictions compared to BMI in the examined diseases and metabolic risk factors (except for stroke in women), while WHR and WSR were better than BMI in some predictions (e.g., hypertension and cardiovascular disease (men); dislipidemia (women); and fasting glucose, diabetes, and stroke (men and women)). There are three potential explanations for the differences. First, the study by Ho et al. (Ho, Lam et al. 2003) was based on a non-representative sample: participants were recruited by telephone (response rate of 78%), and only 38% of responders were examined and included in the final sample. Those participants might have very different disease patterns, risk factors, and health related behaviors compared to the non-participants (Grimes and Schulz 2002). Second, the Ho et al. study (Ho, Lam et al. 2003) included 65–74-year-old participants who might have (a) a lower WC measured at a high location (Ho et al. measured WC at midway between the xiphisternum and the umbilicus) which would underestimate abdominal fat and overestimate the prediction of WC; and (b) a higher BMI due to a biological decrease in height which would underestimate the prediction of BMI. As a result, there would be an increase in the prediction of WC, WSR, or WHR compared to BMI. Third, WC measured in the Ho et al. study was systematically smaller than ours (we measured WC midway between the lowest rib and the iliac crest) (Wang, Thornton et al. 2003). Decreased WSR and WHR, resulting from the smaller WC, would bias the association between WSR and WHR away from the null and would increase their predictions compared to that of BMI.

In the context of a developing country, it is important to find a small number of practical, low cost, and culturally accepted anthropometric indices to predict elevated disease burdens (WHO 2003; Popkin, Kim et al. 2006). In a population or clinical setting among Chinese adults, BMI appears to be sufficient because (a) the exclusion of WC will save time, money, and human resource; (b) the interpretation of a WC value would be confusing because of the lack of a universally accepted site for measuring WC and the large variation of WC optimal cutoffs by sex, age, races, ethnicities, BMI levels, and health outcomes of interest (Klein, Allison et al. 2007). Even in the US, most of the treatment recommendations (99.9% for men and 98.5% for women; data from NHANES III) were based on the evaluation of BMI and cardiovascular risk factors, regardless of the measured WC (Kiernan and Winkleby 2000).

In conclusion, the present study showed that even though WC, WSR, and WHR are predictors of hypertension, they do not perform better than BMI or add to the prediction of hypertension by BMI in Chinese adults. The comparison of PR and AUC, instead of *P*-value or 95% CI, is considered as a strength and a methodological contribution of the study. Further studies with other outcomes (e.g., glucose intolerance, diabetes mellitus, dyslipidemia, and mortality or events of cardiovascular diseases / non-communicable diseases) and more detail information about body composition (e.g., total abdominal adipose tissue, visceral adipose tissue, and total body fat mass) in representative samples of Chinese, other Asian, and Western populations are still needed to confirm the consistency of the finding. Nonetheless, our conclusions about the value of using BMI to predict hypertension are meaningful for decision making in public health and clinical settings. Compared to WC, height and weight and thus BMI (a) are collected more often in nutrition and health surveys, interventions, and in clinics, (b) are collected with the use of universally accepted protocols, and (c) are easier to interpret.

**Table 6.1.** Characteristics of 18–65-year-old Chinese participants

| | Women (n =3,794) | | Men (n = 3,542) | |
|---|---|---|---|---|
| | Estimate | 95%CI | Estimate | 95%CI |
| Age, *y* | 44.0 | (43.6–44.4) | 43.7 | (43.4–44.1) |
| Hypertension | | | | |
| Proportion, *%* | 16.8 | (15.6–18.0) | 23.0* | (21.6–24.4) |
| Diagnosed by a doctor, *%* | 6.6 | (5.8–7.4) | 6.3 | (5.5–7.1) |
| Use anti-hypertensive medication | 5.0 | (4.3–5.7) | 4.1 | (3.4–4.7) |
| Systolic blood pressure, *mm Hg* | 117.8 | (117.3–118.4) | 122.1* | (121.6–122.6) |
| Diastolic blood pressure, *mm Hg* | 76.8 | (76.4–77.1) | 80.1* | (79.8–80.4) |
| Body Mass Index, $kg/m^2$ | 23.1 | (23.0–23.2) | 23.1 | (23.0–23.2) |
| < 18.5 $kg/m^2$, *%* | 6.0 | (5.2–6.7) | 4.9 | (4.2–5.7) |
| ≥ 23 $kg/m^2$, *%* | 46.8 | (45.2–48.4) | 47.1 | (45.4–48.7) |
| ≥ 25 $kg/m^2$, *%* | 27.1 | (25.7–28.5) | 25.5 | (24.1–26.9) |
| Waist circumference, *cm* | 78.7 | (78.4–79.0) | 82.5* | (82.2–82.9) |
| Hip circumference, *cm* | 93.2 | (92.9–93.5) | 94.0* | (93.7–94.3) |
| Waist-to-hip ratio | 0.84 | (0.84–0.85) | 0.88* | (0.88–0.88) |
| Waist-to-stature ratio | 0.50 | (0.50–0.51) | 0.49* | (0.49–0.50) |
| Smoking status | | | | |
| Former smoker, *%* | 0.1 | (0.0–0.2) | 5.6* | (4.8–6.3) |
| Current smoker, *%* | 3.1 | (2.6–3.7) | 58.8* | (57.1–60.4) |
| Alcohol drinker, *%* | 9.0 | (8.0–9.9) | 62.3* | (60.7–63.9) |
| Urban residence, *%* | 34.0 | (32.5–35.5) | 33.9 | (32.3–35.4) |

Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being diagnosed by a doctor. Diagnosed by a doctor: proportion of population that was diagnosed as being hypertensive by a doctor. Use anti-hypertensive medication: proportion of population that used any antihypertensive medications.

* Statistically different compared to women ($P < 0.001$; two-tail t-test for continuous variables or chi squared test for categorized variables).

**Table 6.2.** Sex-specific prevalence ratios of body mass index for hypertension

| | | Women (n = 3,794) | | | | Men (n = 3,542) | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Models** | Independent variables | PR | 95%CI | % change | *P*-value | PR | 95%CI | % change | *P*-value |
| **Crude model** | **BMI** | **1.18** | **(1.16–1.20)** | | | **1.14** | **(1.12–1.17)** | | |
| | BMI + WC | 1.08* | (1.05–1.11) | 8.8 | <0.001 | 1.08* | (1.05–1.11) | 5.7 | <0.001 |
| | BMI + WSR | 1.07* | (1.04–1.11) | 9.5 | <0.001 | 1.06* | (1.03–1.10) | 7.1 | <0.001 |
| | BMI + WHR | 1.15 | (1.13–1.18) | 2.1 | <0.001 | 1.11 | (1.09–1.14) | 2.8 | <0.001 |
| **Age-adjusted** | **BMI** | **1.14** | **(1.11–1.16)** | | | **1.14** | **(1.12–1.16)** | | |
| | BMI + WC | 1.10 | (1.06–1.13) | 3.6 | 0.003 | 1.09 | (1.05–1.12) | 4.7 | <0.001 |
| | BMI + WSR | 1.11 | (1.07–1.14) | 2.6 | 0.029 | 1.09 | (1.06–1.13) | 4.1 | <0.001 |
| | BMI + WHR | 1.13 | (1.11–1.16) | 0.6 | 0.136 | 1.12 | (1.09–1.14) | 2.0 | <0.001 |
| **Age-specific** | **BMI** | **1.16** | **(1.13–1.20)** | | | **1.15** | **(1.12–1.17)** | | |
| | BMI + WC | 1.12 | (1.08–1.16) | 3.7 | 0.002 | 1.09 | (1.06–1.13) | 4.7 | <0.001 |
| | BMI + WSR | 1.13 | (1.09–1.17) | 2.7 | 0.022 | 1.10 | (1.07–1.14) | 4.1 | <0.001 |
| | BMI + WHR | 1.16 | (1.13–1.19) | 0.6 | 0.130 | 1.12 | (1.10–1.15) | 2.0 | <0.001 |

Abbreviations: PR, prevalence ratio of BMI; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WSR, waist-to-stature ratio.
Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being diagnosed by a doctor.
Crude models: include independent variables in the list; crude PR for each unit increase in BMI.
Age-adjusted models: independent variables + age; age-adjusted PR for each unit increase in BMI.
Age-specific model: independent variables + age + (age × BMI); PR for each unit increase in BMI at the age of 45 years.
% Change = 100 × Absolute (LN ($PR_{BMI}$ / $PR_{\text{Test variables}}$)); test variables were BMI + WC, BMI + WSR, or BMI +WHR.
*P*-value: of the increase in model fit compared to a model with BMI (likelihood ratio test).
[*] Statistically different ($P < 0.05$) compared to PR of a model with BMI.

**Table 6.3.** Sex-specific area under the curves (AUC) for the prediction of hypertension by different anthropometric indices

| | | Women (n = 3,794) | | | Men (n = 3,542) | | | Both (n = 7,336) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Models** | Independent variables | AUC | 95%CI | % change | AUC | 95%CI | %change | AUC | 95%CI | %change |
| **Crude model** | **BMI** | **0.71** | **(0.68–0.73)** | | **0.67** | **(0.65–0.69)** | | **0.69** | **(0.67–0.70)** | |
| | WC | 0.72 | (0.69–0.74) | 1.1 | 0.67 | (0.65–0.70) | 0.5 | 0.70 | (0.68–0.71) | 1.9 |
| | WSR | 0.72 | (0.70–0.74) | 2.2 | 0.68 | (0.66–0.70) | 1.7 | 0.69 | (0.68–0.71) | 1.1 |
| | WHR | 0.64* | (0.61–0.66) | 10.4 | 0.64 | (0.62–0.67) | 4.1 | 0.65* | (0.63–0.66) | 5.9 |
| | BMI + WC | 0.73† | (0.70–0.75) | 2.5 | 0.68† | (0.66–0.70) | 1.9 | 0.71† | (0.69–0.72) | 3.0 |
| | BMI + WSR | 0.73† | (0.71–0.75) | 3.4 | 0.69† | (0.67–0.71) | 2.5 | 0.70† | (0.69–0.72) | 2.5 |
| | BMI + WHR | 0.72† | (0.69–0.74) | 1.3 | 0.68† | (0.66–0.71) | 2.0 | 0.70† | (0.69–0.72) | 2.2 |
| **Age-adjusted** | **BMI** | **0.79** | **(0.77–0.81)** | | **0.74** | **(0.72–0.76)** | | **0.76** | **(0.75–0.78)** | |
| | WC | 0.78 | (0.76–0.80) | 1.0 | 0.74 | (0.72–0.76) | 0.8 | 0.76 | (0.75–0.77) | 0.1 |
| | WSR | 0.78 | (0.76–0.80) | 1.5 | 0.73 | (0.72–0.75) | 1.1 | 0.75 | (0.74–0.76) | 1.8 |
| | WHR | 0.75 | (0.73–0.77) | 4.8 | 0.72 | (0.70–0.74) | 3.8 | 0.73* | (0.72–0.75) | 3.8 |
| | BMI + WC | 0.79† | (0.78–0.81) | 0.3 | 0.75† | (0.73–0.77) | 0.7 | 0.77† | (0.76–0.78) | 0.9 |
| | BMI + WSR | 0.79‡ | (0.77–0.81) | 0.2 | 0.75† | (0.73–0.77) | 0.5 | 0.76† | (0.75–0.78) | 0.2 |
| | BMI + WHR | 0.79[ns] | (0.77–0.81) | 0.1 | 0.75† | (0.73–0.77) | 0.6 | 0.77† | (0.75–0.78) | 0.6 |
| **Age-specific** | **BMI** | **0.79** | **(0.77–0.81)** | | **0.74** | **(0.72–0.76)** | | **0.76** | **(0.75–0.78)** | |
| | BMI + WC | 0.79† | (0.78–0.81) | 0.3 | 0.75† | (0.73–0.77) | 0.7 | 0.77† | (0.76–0.78) | 0.9 |
| | BMI + WSR | 0.79‡ | (0.77–0.81) | 0.2 | 0.75† | (0.73–0.77) | 0.5 | 0.76† | (0.75–0.78) | 0.2 |
| | BMI + WHR | 0.79[ns] | (0.77–0.81) | 0.1 | 0.75† | (0.73–0.77) | 0.6 | 0.77† | (0.75–0.78) | 0.6 |

Abbreviations: AUC, area under the curves; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WSR, waist-to-stature ratio.
Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being diagnosed by a doctor.
Crude models: include independent variables in the list
Age-adjusted models: independent variables + age
Age-specific model: independent variables + age + (age × BMI)
% Change = 100 × Absolute (LN ($AUC_{BMI}$ / $AUC_{Test\ variables}$)); test variables were WC, WSR, WHR, BMI + WC, BMI + WSR, or BMI +WHR.
* Statistically different ($P < 0.05$) compared to model with BMI.
† *P*-value < 0.001; ‡ *P*-value < 0.005; [ns] *P*-value = 0.07: the increase in model fit compared to a model with BMI (likelihood ratio test).

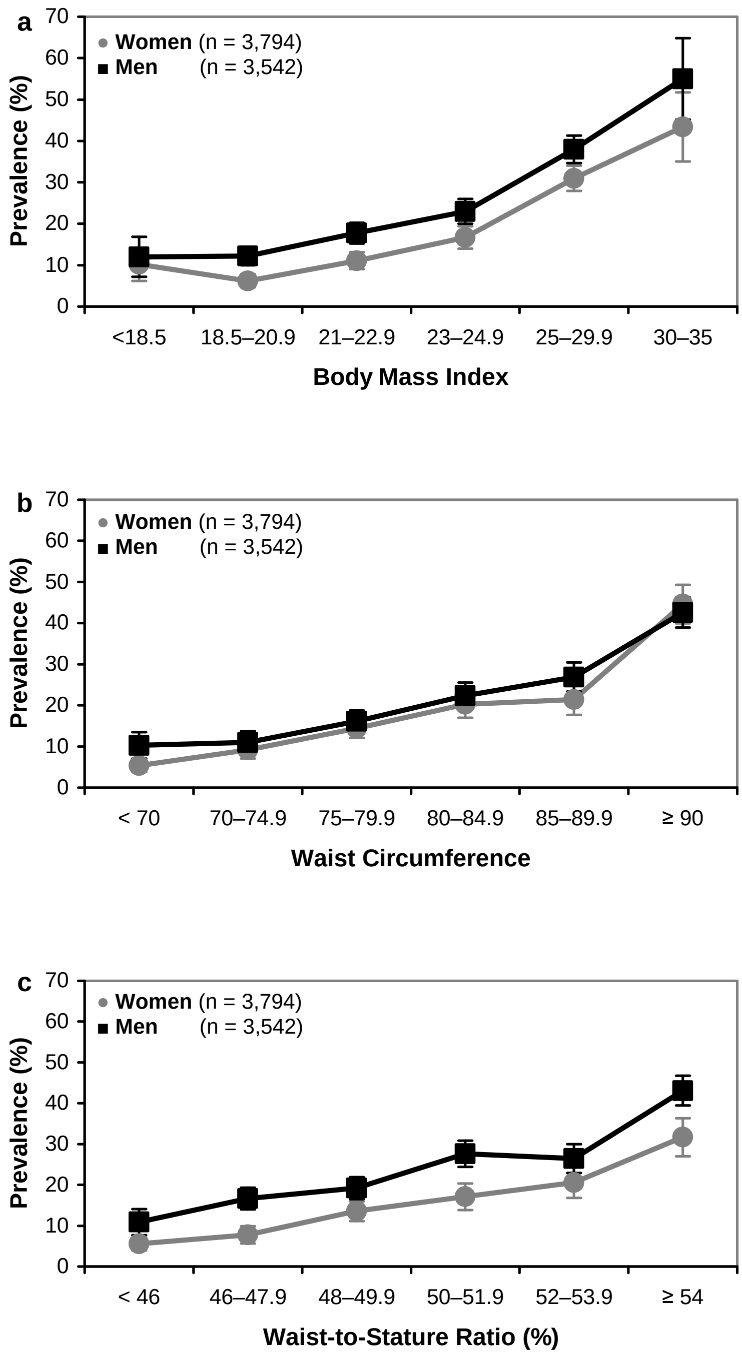


**Figure 6.1.** Prevalence and 95% CI of hypertension by levels of body mass index (*A*), waist circumference (*B*), and waist-to-stature ratio (*C*).
*P* for trend < 0.001 for all

**Supplementary Table 6.1.** Sex-specific prevalence ratios of BMI for hypertension at different BMI levels

| | | Women (n = 3,794) | | | | Men (n = 3,542) | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Models** | Independent variables | PR | 95%CI | % change | P-value | PR | 95%CI | % change | P-value |
| **BMI < 23 kg/m$^2$** | | | | | | | | | |
| **Crude model** | **BMI** | 1.11 | (1.00–1.22) | | | 1.14 | (1.05–1.23) | | |
| | BMI + WC | 1.01 | (0.91–1.12) | 8.8 | <0.001 | 1.06 | (0.97–1.16) | 6.8 | 0.001 |
| | BMI + WSR | 0.99 | (0.90–1.10) | 11.1 | <0.001 | 1.05 | (0.96–1.15) | 7.5 | <0.001 |
| | BMI + WHR | 1.08 | (0.98–1.19) | 2.4 | <0.001 | 1.10 | (1.01–1.20) | 3.2 | 0.002 |
| **Age-adjusted** | **BMI** | 1.07 | (0.98–1.18) | | | 1.12 | (1.04–1.22) | | |
| | BMI + WC | 1.03 | (0.93–1.14) | 4.1 | 0.066 | 1.07 | (0.98–1.17) | 4.7 | 0.021 |
| | BMI + WSR | 1.02 | (0.92–1.13) | 4.7 | 0.027 | 1.09 | (1.00–1.19) | 3.1 | 0.126 |
| | BMI + WHR | 1.06 | (0.97–1.17) | 0.9 | 0.117 | 1.10 | (1.02–1.20) | 1.8 | 0.064 |
| **Age-specific** | **BMI** | 1.00 | (0.89–1.11) | | | 1.10 | (1.01–1.20) | | |
| | BMI + WC | 0.97 | (0.86–1.09) | 3.1 | 0.103 | 1.05 | (0.95–1.15) | 4.8 | 0.021 |
| | BMI + WSR | 0.96 | (0.85–1.08) | 3.7 | 0.044 | 1.06 | (0.97–1.17) | 3.1 | 0.122 |
| | BMI + WHR | 0.99 | (0.88–1.11) | 0.8 | 0.197 | 1.08 | (0.99–1.18) | 1.8 | 0.064 |
| **BMI ≥ 23 kg/m$^2$** | | | | | | | | | |
| **Crude model** | **BMI** | 1.15 | (1.11–1.19) | | | 1.12 | (1.09–1.16) | | |
| | BMI + WC | 1.06 | (1.02–1.11) | 8.1 | <0.001 | 1.07 | (1.03–1.12) | 4.9 | <0.001 |
| | BMI + WSR | 1.07 | (1.02–1.12) | 7.4 | <0.001 | 1.05 | (1.01–1.10) | 6.5 | <0.001 |
| | BMI + WHR | 1.14 | (1.10–1.17) | 1.4 | 0.001 | 1.10 | (1.06–1.14) | 2.4 | <0.001 |
| **Age-adjusted** | **BMI** | 1.12 | (1.09–1.16) | | | 1.13 | (1.09–1.17) | | |
| | BMI + WC | 1.09 | (1.04–1.13) | 3.6 | 0.012 | 1.08 | (1.04–1.13) | 4.4 | 0.001 |
| | BMI + WSR | 1.10 | (1.06–1.15) | 1.8 | 0.192 | 1.08 | (1.04–1.13) | 4.4 | 0.002 |
| | BMI + WHR | 1.12 | (1.08–1.16) | 0.3 | 0.352 | 1.11 | (1.07–1.15) | 2.0 | <0.001 |
| **Age-specific** | **BMI** | 1.15 | (1.10–1.20) | | | 1.14 | (1.10–1.18) | | |
| | BMI + WC | 1.11 | (1.06–1.17) | 3.6 | 0.013 | 1.09 | (1.05–1.14) | 4.3 | 0.001 |
| | BMI + WSR | 1.13 | (1.08–1.19) | 1.8 | 0.190 | 1.09 | (1.05–1.14) | 4.3 | 0.002 |
| | BMI + WHR | 1.15 | (1.10–1.20) | 0.4 | 0.369 | 1.12 | (1.08–1.16) | 2.0 | <0.001 |

Abbreviations: PR, prevalence ratio of BMI; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WSR, waist-to-stature ratio.
Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being diagnosed by a doctor.

| | |
|---|---|
| Crude models: | include independent variables in the list; crude PR for each unit increase in BMI. |
| Age-adjusted models: | independent variables + age; age-adjusted PR for each unit increase in BMI. |
| Age-specific model: | independent variables + age + (age × BMI); PR for each unit increase in BMI at the age of 45 years. |

% Change = 100 × Absolute (LN ($PR_{BMI}$ / $PR_{Test\ variables}$)); test variables were BMI + WC, BMI + WSR, or BMI +WHR.
*P*-value: of the increase in model fit compared to a model with BMI (likelihood ratio test).
[*] Statistically different ($P < 0.05$) compared to PR of a model with BMI.

**Supplementary Table 6.2.** Sex-specific area under the curves (AUC) for the prediction of hypertension by different anthropometric indices at different BMI levels

| | | Women (n = 3,794) | | | Men (n = 3,542) | | | Both (n = 7,336) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Models** | Independent variables | AUC | 95%CI | % change | AUC | 95%CI | %change | AUC | 95%CI | %change |
| **BMI < 23 kg/m$^2$** | | | | | | | | | | |
| **Crude model** | **BMI** | 0.56 | (0.51–0.60) | | 0.57 | (0.53–0.61) | | 0.57 | (0.54–0.60) | |
| | WC | 0.61 | (0.57–0.66) | 9.3 | 0.60 | (0.56–0.63) | 4.5 | 0.62 | (0.59–0.65) | 8.7 |
| | WSR | 0.65 | (0.61–0.69) | 15.3 | 0.60 | (0.56–0.64) | 5.5 | 0.61 | (0.59–0.64) | 7.8 |
| | WHR | 0.60 | (0.56–0.64) | 6.9 | 0.58 | (0.54–0.62) | 2.0 | 0.60 | (0.57–0.63) | 6.0 |
| | BMI + WC | 0.61† | (0.57–0.66) | 9.3 | 0.60† | (0.56–0.63) | 4.8 | 0.62† | (0.59–0.65) | 8.6 |
| | BMI + WSR | 0.65*,† | (0.61–0.69) | 15.5 | 0.60† | (0.56–0.64) | 5.5 | 0.61† | (0.58–0.64) | 7.7 |
| | BMI + WHR | 0.60† | (0.56–0.64) | 7.0 | 0.59‡ | (0.55–0.62) | 3.2 | 0.61† | (0.58–0.63) | 6.8 |
| **Age-adjusted** | **BMI** | 0.77 | (0.74–0.80) | | 0.70 | (0.66–0.73) | | 0.73 | (0.70–0.75) | |
| | WC | 0.77 | (0.74–0.81) | 0.4 | 0.70 | (0.67–0.73) | 0.8 | 0.74 | (0.71–0.76) | 1.0 |
| | WSR | 0.77 | (0.74–0.81) | 0.4 | 0.70 | (0.66–0.73) | 0.2 | 0.73 | (0.71–0.75) | 0.0 |
| | WHR | 0.77 | (0.74–0.81) | 0.2 | 0.70 | (0.66–0.73) | 0.2 | 0.73 | (0.71–0.76) | 0.6 |
| | BMI + WC | 0.77‡ | (0.74–0.81) | 0.3 | 0.70‡ | (0.67–0.73) | 0.9 | 0.74† | (0.71–0.76) | 1.0 |
| | BMI + WSR | 0.77‡ | (0.74–0.81) | 0.5 | 0.70 | (0.67–0.73) | 0.5 | 0.73‡ | (0.71–0.75) | 0.3 |
| | BMI + WHR | 0.77 | (0.74–0.81) | 0.3 | 0.70‡ | (0.67–0.73) | 0.6 | 0.73† | (0.71–0.76) | 0.8 |
| **Age-specific** | **BMI** | 0.78 | (0.74–0.81) | | 0.70 | (0.66–0.73) | | 0.73 | (0.71–0.75) | |
| | BMI + WC | 0.78 | (0.75–0.81) | 0.2 | 0.70‡ | (0.67–0.73) | 0.9 | 0.74† | (0.71–0.76) | 1.1 |
| | BMI + WSR | 0.78‡ | (0.75–0.81) | 0.2 | 0.70 | (0.67–0.73) | 0.5 | 0.73‡ | (0.71–0.76) | 0.3 |
| | BMI + WHR | 0.78 | (0.75–0.81) | 0.2 | 0.70‡ | (0.67–0.73) | 0.6 | 0.74† | (0.71–0.76) | 0.9 |
| **BMI ≥ 23 kg/m$^2$** | | | | | | | | | | |
| **Crude model** | **BMI** | 0.65 | (0.62–0.68) | | 0.63 | (0.60–0.66) | | 0.64 | (0.62–0.66) | |
| | WC | 0.66 | (0.64–0.69) | 1.9 | 0.63 | (0.60–0.66) | 0.3 | 0.65 | (0.63–0.67) | 2.6 |
| | WSR | 0.66 | (0.63–0.69) | 1.3 | 0.65 | (0.62–0.68) | 3.0 | 0.64 | (0.62–0.66) | 1.0 |
| | WHR | 0.59 | (0.56–0.62) | 9.5 | 0.62 | (0.59–0.65) | 1.9 | 0.61 | (0.59–0.63) | 4.1 |
| | BMI + WC | 0.67† | (0.64–0.70) | 3.2 | 0.65† | (0.62–0.68) | 2.8 | 0.66† | (0.64–0.68) | 4.0 |
| | BMI + WSR | 0.67† | (0.64–0.70) | 3.0 | 0.66† | (0.63–0.68) | 4.0 | 0.66† | (0.64–0.68) | 2.8 |
| | BMI + WHR | 0.66† | (0.63–0.69) | 0.7 | 0.65† | (0.63–0.68) | 3.9 | 0.66† | (0.64–0.68) | 2.9 |

| | | Women (n = 3,794) | | | Men (n = 3,542) | | | Both (n = 7,336) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Models** | Independent variables | AUC | 95%CI | % change | AUC | 95%CI | %change | AUC | 95%CI | %change |
| **Age-adjusted** | **BMI** | 0.74 | (0.72–0.77) | | 0.72 | (0.69–0.74) | | 0.72 | (0.70–0.74) | |
| | WC | 0.73 | (0.71–0.76) | 1.1 | 0.71 | (0.69–0.74) | 0.6 | 0.72 | (0.71–0.74) | 0.2 |
| | WSR | 0.73 | (0.70–0.75) | 2.3 | 0.71 | (0.69–0.74) | 0.3 | 0.71 | (0.69–0.73) | 2.0 |
| | WHR | 0.71 | (0.68–0.73) | 4.8 | 0.70 | (0.67–0.73) | 2.3 | 0.70 | (0.68–0.72) | 2.9 |
| | BMI + WC | 0.75[‡] | (0.72–0.77) | 0.5 | 0.72[†] | (0.70–0.75) | 1.1 | 0.73[†] | (0.71–0.75) | 1.4 |
| | BMI + WSR | 0.74 | (0.72–0.77) | 0.1 | 0.72[†] | (0.70–0.75) | 1.1 | 0.72[‡] | (0.71–0.74) | 0.3 |
| | BMI + WHR | 0.74 | (0.72–0.77) | 0.0 | 0.73[†] | (0.70–0.75) | 1.5 | 0.73[†] | (0.71–0.75) | 1.1 |
| **Age-specific** | **BMI** | 0.74 | (0.72–0.77) | | 0.72 | (0.69–0.74) | | 0.72 | (0.70–0.74) | |
| | BMI + WC | 0.75[‡] | (0.72–0.77) | 0.5 | 0.72[†] | (0.70–0.75) | 1.1 | 0.73[†] | (0.71–0.75) | 1.5 |
| | BMI + WSR | 0.74 | (0.72–0.77) | 0.1 | 0.72[†] | (0.70–0.75) | 1.2 | 0.72[‡] | (0.71–0.74) | 0.3 |
| | BMI + WHR | 0.74 | (0.72–0.77) | 0.0 | 0.73[†] | (0.70–0.75) | 1.5 | 0.73[†] | (0.71–0.75) | 1.1 |

Abbreviations: AUC, area under the curves; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WSR, waist-to-stature ratio.
Hypertension was defined as a systolic blood pressure ≥ 140, a diastolic blood pressure ≥ 90 mmHg, or being diagnosed by a doctor.
Crude models: include independent variables in the list
Age-adjusted models: independent variables + age
Age-specific model: independent variables + age + (age × BMI)
% Change = 100 × Absolute (LN ($AUC_{BMI}$ / $AUC_{Test\ variables}$)); test variables were WC, WSR, WHR, BMI + WC, BMI + WSR, or BMI +WHR.
[*] Statistically different ($P$ < 0.05) compared to model with BMI.
[†] $P$-value < 0.001; [‡] $P$-value < 0.005; [ns] $P$-value = 0.07: the increase in model fit compared to a model with BMI (likelihood ratio test).

# CHAPTER 7. SYNTHESIS

## 7.1. Overview of findings

This research investigates the BMI–hypertension relationship in Chinese, Indonesian, and Vietnamese adults. We used data from the China Health and Nutrition Survey (CHNS in 2000 and 2004), the Indonesian Family Life Survey (IFLS in 2000), and the Vietnam National Health Survey (VNHS in 2002). These surveys were designed to study the health and nutritional status of the corresponding populations. In the surveys, blood pressure and anthropometric measures were collected by trained health workers who followed a standardized procedure using regularly calibrated equipment. With the use of criteria that are less affected by sample sizes (e.g., an ROC curve analysis), first, we compared the association between BMI and hypertension among 18–65-year-old Chinese, Indonesian, and Vietnamese adults and determined optimal BMI cutoffs for those populations. Second, we compared the prediction of hypertension by waist circumference (WC), waist-to-stature ratio (WSR), or waist-to-hip ratio (WHR) to that by BMI and determined if WC, WSR, or WHR added to the prediction of hypertension by BMI in Chinese adults. Finally, we aimed to increase the scope of our earlier analyses by including a prospective longitudinal sample that allowed us to determine an optimal BMI cutoff as a screening threshold for elevated incidence of hypertension in Chinese adults. Below, we briefly summarize our findings and then provide a synthesis of our overall research.

### *7.1.1. East and Southeast Asians are different in the association between body mass index and hypertension*

Using three representative samples in the early 2000s, our objectives were to compare the association between BMI and hypertension among 18–65-year-old Chinese, Indonesian, and Vietnamese adults and to determine optimal BMI cutoffs for those populations. We hypothesized that Chinese, Indonesian, and Vietnamese adults require different optimal BMI cutoffs and respond differently to an increase in BMI.

The inclusion of different Asian populations in this study allowed us to directly compare the association between BMI and hypertension between the Chinese, Indonesians, and Vietnamese and to examine whether a country-specific or even country-, sex-, age-specific BMI cutoffs are needed. Our study enriched current knowledge by providing information about optimal BMI cutoffs for Southeast Asian populations.

Although optimal BMI cutoffs are all < 25 kg/m$^2$, the study showed ethnic differences in the BMI-hypertension association and in optimal BMI cutoffs between Chinese, Indonesian, and Vietnamese adults. The study also showed a variation in optimal BMI cutoffs by sex and age between and within the ethnicities. The study suggested the need of country-specific and even country-, sex-, and age-specific BMI cutoffs to identify people at high risk of cardiovascular diseases.

### *7.1.2. Longitudinal association between body mass index and hypertension in Chinese adults*

Using data from the CHNS 2000–2004 cohort, our objectives were to examine the longitudinal association between BMI and hypertension and to determine an optimal BMI cutoff based on cumulative incidence of hypertension among Chinese adults. We hypothesized that Chinese adults have increased incidence of hypertension at BMI of less than 25 kg/m$^2$.

We are the first to use a receiver operating characteristic (ROC) curve to evaluate an optimal BMI cutoff in an Asian longitudinal sample. This cohort allowed us to estimate an optimal BMI cutoff based cumulative incidence of hypertension. An ROC curve analysis, which is less affected by sample size compared to a *P*-value, is currently considered a better approach to determine an optimal BMI level. It is also a unique opportunity for us to compare optimal BMI cutoffs based on this longitudinal sample to those obtained from a cross-sectional sample (e.g., the CNHS in 2004). The comparison allowed us to suggest a certain adjustment to an optimal BMI level obtained from a cross-sectional study.

In this cohort, we found an optimal BMI value of about 23.0 kg/m$^2$ (22.5 kg/m$^2$ for men and 22.5 kg/m$^2$ for women) to be used in the Chinese adults to identify the increased incidence of hypertension. The optimal BMI cutoff from the CHNS 2000–2004 cohort is about 0.5–1.0 unit smaller than that obtained from the cross-sectional sample of the CHNS in 2004.

### *7.1.3. Prediction of hypertension by different anthropometric indices in Chinese adults*

Using data from the CHNS in 2004, our objectives were to compare the prediction of hypertension by WC, WSR, or WHR to that by BMI and to determine if WC, WSR, or WHR adds to the prediction of hypertension by BMI among 18–65-year-old Chinese adults. We hypothesized that at a population level, WC, WHR, and WSR do not add significantly to the prediction of hypertension by BMI.

To answer the research question, we are the first to use the change-in-estimate approach, which is more stable to sample sizes compared to methods that had been used by other authors (e.g., a *P*-value < 0.05 or a non-overlap of 95% CI). The approach allowed us to examine whether predictions of a health outcome by anthropometric indices are meaningfully different (e.g., a ≥ 10% difference in estimates), not statistically different (e.g., a *P*-value < 0.05).

Based on the change in prevalence ratio or area under the curve, WC, WSR, and WHR did not perform better than BMI or add to the prediction of hypertension by BMI. BMI appears to be sufficient to screen for increased prevalence of hypertension among 18–65-year-old Chinese adults. The finding is beneficial for decision makers in a developing country because it narrows down the list of anthropometric indices to be collected to predict and monitor elevated risk of non-communicable diseases (NCDs).

## 7.2. Public health significance

The study was conducted to determine BMI cutoffs for overweight based on both cross-sectional and longitudinal samples and to determine the best anthropometric index to be used in Asian populations.

### *7.2.1. Our findings suggest an optimal BMI cutoff of < 25 kg/m$^2$ for Asian populations*

With the use of ROC curve analyses, both longitudinal and cross-sectional studies suggest an optimal BMI cutoff of < 25 kg/m$^2$ in the studied populations. The use of large and representative samples from recent nutrition and health surveys allows for the generalizability of these findings to the corresponding populations.

Our findings support the recommendation of the WHO for an optimal BMI cutoff for Asians. The recommendation of a lower optimal BMI level is beneficial for Asians because it triggers earlier preventions of excessive weight gains and NCDs. Asians, who are living mostly in developing countries with inadequate lifestyle and medication treatments for hypertension as well as other CVD risk, are more susceptible to health consequences of elevated blood pressures (e.g., renal and heart failure, stroke, and heart attach) compared to Westerners. Also, because of the less effective treatments for CVD events and rehabilitation, the CVD events are usually link to higher rate of death and disability that reduce quality of lives. Thus, maintaining a lower BMI level will help to reduces economic and health burdens of overweight and NCDs among Asians worldwide. Because elevation in BMI is only one of the NCD risk factors, other risk factors such as smoking, excessive alcohol consumption, salty and fatty food intakes, and low physical activity level should also be included in the intervention policy.

#### *7.2.2. Our findings suggest the need of a country-specific BMI cutoff for Asians*

Optimal BMI cutoffs appear to be varied among Asians. The finding is reasonable because Asians have many sub-ethnic groups that are different in both individual and environmental backgrounds such as body compositions, genotypes, lifestyles, age structures, cultures, religions, and socio-economic status. In our study, the suggestion of a country-specific BMI cutoff is supported by the differences in association between BMI and hypertension between Chinese, Indonesian, and Vietnamese adults. The differences are consistent in both sex-specific crude and age adjusted estimates (e.g., prevalence and risk ratios).

In addition, we also found a variation in optimal BMI cutoffs by sex and age within each ethnicity. Thus, a country-specific or even country-, sex-, age-specific optimal BMI cutoffs are needed. Those specific BMI cutoffs allow policy makers from each country to have a timely intervention. Stratification of the analyses by sex and are needed to address the differences in sex and age structures of the study populations.

Although the WHO/IASO/IOTF found certain differences among Asians, and between sex and age groups, they tended to suggest a combined optimal BMI cutoff for Asians, the recommendation makes it easier for a public recommendation about an optimal weight in Asians. It, however, does not capture the differences among regions (e.g., Eastern, Southeast, South, or Middle East) and countries in Asia; or between different ethnic, age, and sex groups within each country. We are arguing for an optimal BMI cutoff for Asians that is lower compared to that of Westerners to address the increased risk of NCDs. Based on the same argument, ones might argue about a more specific BMI cutoff.  However, the stratification would lead to a more complicated message. Regardless of any specific BMI cutoffs, every countries should report nutrition status of adults using international BMI cutoffs (e.g., 25 kg/m$^2$ for overweight and 30 kg/m$^2$ for obesity) to facilitate inter-country comparison.

### *7.2.3. Our findings suggest that BMI is sufficient to screen for cardiovascular risk in Asians*

Our findings show that WC, WSR, and WHR do not perform better than BMI or add meaningfully to the prediction of hypertension outcome by BMI. Compared to WC, height and weight and thus BMI (a) are collected more often in nutrition and health surveys, interventions, and in clinics, (b) are collected with the use of universally accepted protocols, (c) are easier to interpret, and (d) are used more regularly in clinical decisions. In addition, the exclusion of WC helps to save time, money, and human resources that are important for a lower income country.

#### *7.2.4. Our study suggests adjustments for BMI cutoffs estimated from a cross-sectional study*

Based on the CHNS longitudinal sample, our findings suggest a 0.5–1.0 kg/m$^2$ subtraction from the optimal BMI cutoff obtained from the CHNS 2004 cross-sectional sample. Although the observation should be carefully verified by conducting a similar study with the use of different longitudinal CVD outcomes, the information is needed to develop an optimal BMI cutoff for a population where a longitudinal sample is not available.

### 7.3. Strengths and limitations

#### *7.3.1. Strengths*

In this research, we were able to use large and representative samples from nutrition and health surveys conducted in China, Indonesia, and Vietnam in the early 2000s. The use of the data allowed us to (a) provide precise and representative estimations of prevalence, incidence, prevalence ratios, risk ratios, and BMI cutoffs; (b) stratify our analyses by sex and age groups; and (c) compare and contrast the associations between BMI and hypertension as well as BMI cutoffs within Asians. The study also enriches current knowledge by providing information about the association between BMI and hypertension in Southeast Asians.

In the research, we also had a unique opportunity to determine BMI cutoffs based on the incidence of hypertension. Going beyond a cross-sectional study, starting with normotensive participants, we were able to evaluate a temporary criterion, one of the most important criteria in assessing a causal relationship. With the longitudinal sample, we could test the effect of a higher BMI to an increase in blood pressure and screen out the reversed direction (e.g., a hypertensive patient would have modified his lifestyles that lead to a reduction of body weight, and thus BMI).

The other strength of this study is that blood pressure and anthropometric measures were collected by trained health workers who follow standardized protocols; other covariates were obtained from direct interviews. The direct measurements provided more reliable and comparable measures compared to those from self-reported methods, which are usually affected by measurement errors (e.g., poorly standardized equipments and variations in measurement skills) and information bias (e.g., rounding, recalling, and reporting errors).

In this study, we used criteria that are more stable to sample sizes compared to methods that had been used by other authors (e.g., a $P$-value < 0.05 or a non-overlap of 95% CI). For example, to determine an optimal BMI cutoff, we used an ROC curve analysis to find the largest sensitivity and specificity; and to define the best anthropometric index, we compared values of area under the curve (AUC) or prevalence ratios (PR). The new approaches would be used to analyze data from different countries to give comparable findings.

### *7.3.2. Limitations*

Study design

We would have performed more indepth analyses if the number of participants in each survey had been sampled proportionally to the country's population. For example, within the three countries, although China is the most populous, the sample size of the CHNS is the smallest; while Vietnam is the least populous, the sample size of the VNHS is the largest. Because of the limitation, we were not able to pool the three data sets together to perform indepth analyses or to define a general optimal BMI cutoff for the three countries.

We were not able to obtain any survey or weighted estimates in Chinese adults because no sampling weights were assigned to the data from CHNS. We, however, expect that the point estimates of all analyses in Chinese adults were similar to those if a weighted estimation had been assigned because there was not any group that had been over-sampled in the CHNS. The CHNS used a weighted sampling scheme to select randomly counties and cities in each province; and then villages and townships within the counties or cities. We, however, expect that the 95% CI range would have been larger if a survey command had been used to analyze data from the CHNS.

*Study variables*

There are two factors, which would cause a systematic difference in values of blood pressure measured in different countries. First, the surveys used different types of sphygmomanometers to measure blood pressure. However, the differences in equipment are unlikely to alter prevalence of hypertension. First, these surveys followed a standardized protocol in measuring blood pressures. Second, the regularly calibrated sphygmomanometers used in these surveys are in the list of recommended equipment. Finally, the rounding error in measuring blood pressure was not an issue in any surveys. Second, blood pressure, measured only one time in the IFLS would be systematically elevated compared to the mean three measurements (if they had been ideally collected). Sensitivity analysis showed no effect of the potential elevation in blood pressure on any predictions (e.g., PR, AUC, BMI cutoffs) and overall conclusions.

Some covariates such as smoking, alcohol drinking habits, dietary intakes, physical activities, were not measured in the same way across surveys. In addition, the definition of some variables such as urbanization levels, education levels, and economic status were characterized differently in different surveys. Although those variables did not confound or modify the association between BMI and hypertension within a country, it is unclear if can they would explain differences between countries.

*The use of ROC curve approach*

The use of an ROC curve analyses appears to be a better approaches compared to the use of a *P*-value or 95% CI in the determination of an optimal cutoff (e.g., of an anthropometric index) for a certain health condition. There are also some concerns about the use of an ROC curve. First, it depends largely on the AUC values that ranged from 1.0 for a perfect prediction to 0.5 for no prediction. In the study, although the AUC values of 0.6–0.8 suggest that BMI predict well hypertension, we are not sure if an optimal BMI cutoff would have the same meaning between groups that have substantial differences in prediction of a disease outcome by BMI (e.g., indicating by the difference in AUC values).

Second, the sensitivity and specificity of a screening test (in this case, a BMI level to predict a disease risk) depend on distributions of exposure, outcome, and other covariates (e.g., factors at individual or environmental levels). For example, given all other factors constant, an increase in mean BMI leads to an increase in optimal BMI cutoffs. On the other hand, an increase in cardiovascular risk, which is associated with an increase in BMI, allows us to detect elevated a cardiovascular risk at a lower BMI, and thus, leads to a decrease in optimal BMI cutoff. In combination with other complex changes or differences in environmental factors, although we knew the difference in mean BMI of given populations, we are not able to predict the difference in optimal BMI cutoff. Thus, the ethnic or country specific BMI cutoff should be understood as the combination of all factors.

Finally, although we could see a large difference in sensitivity and specificity between a BMI level of 23 and 25 kg/m$^2$ in the Asian populations, we did not see any substantial difference in sensitivity and specificity within 0.5 unit of BMI (e.g., 22.5, 23, and 23.5 kg/m$^2$). Thus, it might be acceptable for a slightly higher or lower BMI level. We, however, think a lower BMI level (priority on sensitivity) for the detection of a disease risk should be used, because (a) both overweight and NCD risk are preventable and treatable and (b) the early prevention of overweight and NCD risk is a cost-benefit means to reduce economic and health burdens of obesity and NCD.

*Finding generalizability*

Although this research suggests a good generalizability within study, there are some factors that affect the inter study validation. First, the findings are based on hypertension as study outcome. With other outcomes, we might found a different BMI cutoff. Also, we are not sure if WC predicts diabetes mellitus better than BMI or adds to the prediction of hypertension by BMI. Since WC is felt to be more predictive of visceral fat than BMI, WC might be more linked with diabetes mellitus than BMI. Second, our sample did not include participants from all Asian regions. Different sub-ethnic groups within Asian might have very different association between an anthropometric index and a disease risk or health outcome, and thus, different cutoff for the anthropometric index. In addition, in this sample, we included only 18–65-year-old adults. Thus, the finding about the optimal BMI cutoff or the association between BMI and WC with a health outcome is not ready to be used for an older or younger participant.

### 7.4. Directions for future research

The use of ROC curve analyses in a longitudinal study and the use of the change-in-estimate approach to define the best anthropometric index appear to be a good approach to define an optimal BMI cutoff. The approaches could be used in further studies with representative longitudinal samples in different Asian populations and with other outcomes (e.g., incidence of diabetes mellitus, dyslipidemia, and cardiovascular disease events or mortality). The study might also include samples from Western populations to enable direct comparison. The multi-country study should have similar sampling strategy and with sample sizes proportional to population size; it should follow the same protocol in measuring key variables of interests.

Further study should take into account genetic, individual, and environmental factors to explore the complex association between BMI and non-communicable diseases. The research would help to cluster populations / ethnicities by their similarities and genotypes, and gene-environment interactions. The recommendation of an optimal BMI cutoff would be more informative within clusters of these populations.

Although there are still some methodological limitations, this study, along with other studies indicate that Asians developed NCDs at a lower BMI compared to other ethnicities. A recommendation of a lower BMI cutoff helped to reduce morbidity and mortality among Asians, and thus, helps to reduce disease burdens in Asia and in the world. It would be more meaningful to focus on how to implement both country and international BMI cutoffs in one country and to evaluate the benefit of a lower BMI cutoff in nutrition, health, and economic status in certain populations.

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